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The Journal is the official organ of the American Academy of Periodontology and will contain, therefore, papers of scientific and clinical interest which are presented at the annual meetings of that society, as well as articles submitted direct to the Editor. Obviously opinions expressed do not necessarily represent those of the Editor or the American Academy of Periodontology.

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April 24 - 26, 1961

Ann Arbor, Michigan

B. O. A. THOMAS, D.D.S., Ph.D.

1960-61 President, American Academy of Periodontology

Dr. B. O. A. Thomas, of Palo Alto, California, is President of the American Academy of Periodontology during 1961. He also serves as Secretary-Treasurer of the American Board of Periodontology. In addition, he is President-Elect of The California Academy of Periodontology and President of the Mid-Peninsula Dental Society (California).

Dr. Thomas spent his youth in North Dakota and graduated from the University of Minnesota (D.D.S., 1935; B.A., 1936; M.S., 1939). He then went to Columbia University (D.D.S., 1940; Ph.D., 1946), during which period he taught at Columbia's School of Dental and Oral Surgery, in the fields of Oral Histology and Operative Dentistry. In 1946 he became the first faculty member at the new School of Dentistry, the University of Washington, Seattle. There he served as Professor and Executive Officer of the Department of Periodontology until 1956, at which time he moved to Palo Alto, California, where he conducts a private practice, limited to periodontics. Dr. Thomas continues his interest in education by part-time teaching at The College of Physicians and Surgeons Dental School, San Francisco (Clinical Professor of Periodontics) and at Stanford University Medical School, Palo Alto (Lecturer in Anatomy). In addition, he is a member of the Postgraduate Faculty, University of Oregon Dental School, Portland.

Dr. Thomas serves as Area Consultant in Periodontics for the Veterans Administration and holds the rank of Commander in the Dental Corps of the U.S. Naval Reserve.

THE JOURNAL OF PERIODONTOLOGY

JANUARY, NINETEEN HUNDRED SIXTY ONE

Histologic and Histochemical Observations Regarding Early Calculus Formation in Children and Adults

by SAMUEL TURESKY, GRETE RENSTRUP AND IRVING GLICKMAN, *Boston, Massachusetts*

THE study of calculus formation received new impetus in 1957 when Mandel, Levy and Wasserman[1] reported their *in vivo* celluloid strip technique for collecting calculus. Since that time, the histological and histochemical features of early calculus formation have been described in several reports. There has been general agreement that calculus begins as a soft adherent bacterial-laden plaque which undergoes progressive calcification. Observations and opinions regarding the chemical nature of the plaque, the bacterial components, and the process of mineralization have been reviewed by Wah Leung.[2] We were interested in determining a) whether additional information regarding calculus formation could be derived from further microscopic and histochemical studies of calculus obtained in humans and b) whether there were differences between calculus formation in children and adults.

EXPERIMENTAL PROCEDURE

To collect the calculus, sections of cellulose acetate crowns were tailored onto the lingual surface of mandibular incisors and tied into position with ligature wire so that one edge extended into the gingival sulcus. Seventy four males and females, ages 5 to 70 served as experimental subjects. Of these, fourteen were between the ages of five and twelve. Three or four strips were placed in each subject, with instructions to avoid toothbrushing in the area. Smooth strips and strips roughened with sandpaper discs were used. The strips were removed at intervals from 1 to 30 days so that the accumulated deposits could be studied grossly and microscopically. A total of 244 strips were examined.

Upon removal from the oral cavity, each strip was divided in half. One half was fixed in 10% formalin, the other half in a 1% solution of trichloracetic acid in 80% alcohol. After twenty four hours of fixation the strips were embedded in paraffin and sectioned serially at a thickness of 7 to 10 mu.

The following histochemical techniques were used in the preparation of the microscopic sections of the formalin fixed specimens: 1) the periodic acid-Schiff

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(P.A.S.) technique[3] to demonstrate glycogen and carbohydrate-protein complexes; 2) the Barrnett-Seligman technique[4] for the demonstration of protein-bound sulfhydryl- and disulfide-groups; 3) toluidine-blue (0.05%, pH 7.1) to demonstrate metachromasia; 4) and 5) alizarin[5] and von Kossa[6] silver stains to demonstrate calcification. A serial section of each specimen was stained with hematoxylin and eosin for the purpose of orientation.

The specimens fixed in trichloracetic acid were treated the same as those above except that the Gram stain was omitted and the Weiss, Tsou, Seligman technique[7] for demonstrating protein-bound amino groups was added.

Specimens were treated with oxalic acid (2%) to test for the presence of calcium. To eliminate crystals of oxalic acid, the slides were treated with ammonium hydroxide (0.5%). The hexagonal crystals which remained were assumed to be calcium-oxalate. Sections were also studied under polarized light for the presence of birefringent crystals.

Fig. 1. Strip removed after two weeks in the mouth, showing the distribution of the accumulated calculus. Note the absence of calculus on the lower border of the strip which was inserted beneath the margin of the gingiva.

GROSS OBSERVATIONS

Soft material accumulated on the strips in the form of an adherent plaque on the entire surface, and was present in greatest amounts near the gingival margin. There was no accumulation on the portion of the strip inserted below the gingival margin into the gingival sulcus (Fig. 1). Plaque accumulated earlier in the experiment and in greater amounts on the roughened strips. The amount of accumulation varied in different mouths and in different strips in the same mouth. The plaque ranged in color from white to yellowish brown. It underwent progressive hardening in most instances. The plaque adhered to the strips when they were removed from the teeth for processing.

MICROSCOPIC FINDINGS

The soft plaque consisted for the most part of bacteria with a scattering of leukocytes and epithelial cells contained within an amorphous matrix. Initial microscopic evidence of calcification occurred in the form of foci located near or on the strip surface. As calcification progressed the foci increased in size and coalesced to form a continuous mass. There was no relationship between the amount of accumulation and the time of onset of calcification. In the 13 to 70 year age group there was microscopic evidence of calcification in all specimens between the second and sixteenth day. By the eighth day, 85% of the specimens had undergone some degree of calcification. In the 5 to 12 year age group, no calcification occurred during the 30 day experimental period in 4 out of 14 subjects. In the remaining subjects the time of calcification was essentially the same as that observed in the older group.

The amount of accumulated calculus in

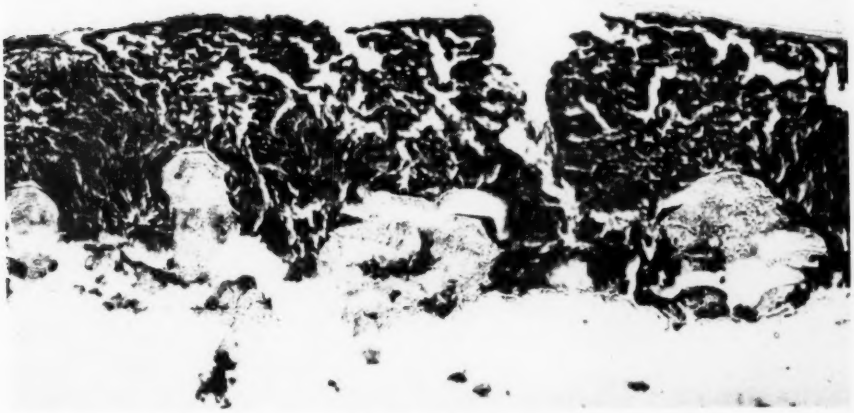

Fig. 2. Five day plaque with foci of calcification which are unstained with toluidine blue. Orig. Mag. 100X.

the course of the experimental period was greater in the older age groups. However, the staining qualities and bacterial components and the microscopic changes associated with calcification were similar in both groups.

Calcification of the plaque was accompanied by changes in the stain qualities and bacterial content. In specimens without microscopic evidence of calcification the plaque stained basophilic with hematoxylin and eosin. It was P.A.S. positive indicating the presence of carbohydrate-protein complexes. The P.A.S. staining was unaffected by treatment with diastase, indicating an absence of glycogen. Protein bound sulhydryls, disulfides and amino groups were present throughout the plaque. With toluidine blue the plaque stained orthochromatic. It was not possible to establish the extent to which the staining qualities of the plaque were determined by the matrix or the bacteria.

Alterations in the staining of the plaque occurred associated with calcification in the focal areas. There was a change from basophilia to eosinophilia. The staining of P.A.S.-positive groups, sulfhydryl and amino groups was reduced. The intensity of the Gram stain was also diminished. The staining with toluidine blue, initially orthochromatic became metachromatic and disappeared in the foci (Fig. 2). Some of the foci contained numerous small metachromatic spherical masses (Fig. 3). At the periphery of the foci the intensity of the P.A.S. stain was often increased.

The calcified foci stained black with von Kossa's silver stain (Fig. 4), and orange red with alizarin-red. Areas within calcification foci were birefringent.

The Microbial Component of the Plaque. Non-calcified plaques consisted of a dense meshwork of diffusely distributed Gram-negative cocci with occasional rod forms almost to the exclusion of other microorganisms (Fig. 5). In some instances there were a few isolated clumps of Gram-positive cocci. Filamentous or thread shaped organisms were scarce in the non-calcified plaques.

The bacterial content of the plaque changed with the occurrence of calcification. Gram-negative filaments and threads became prominent throughout the specimen (Fig. 6) and increased in number as calcification progressed until they equalled or exceeded the other bacteria. The filaments and threads were located on the strip surface, centrally within the plaque

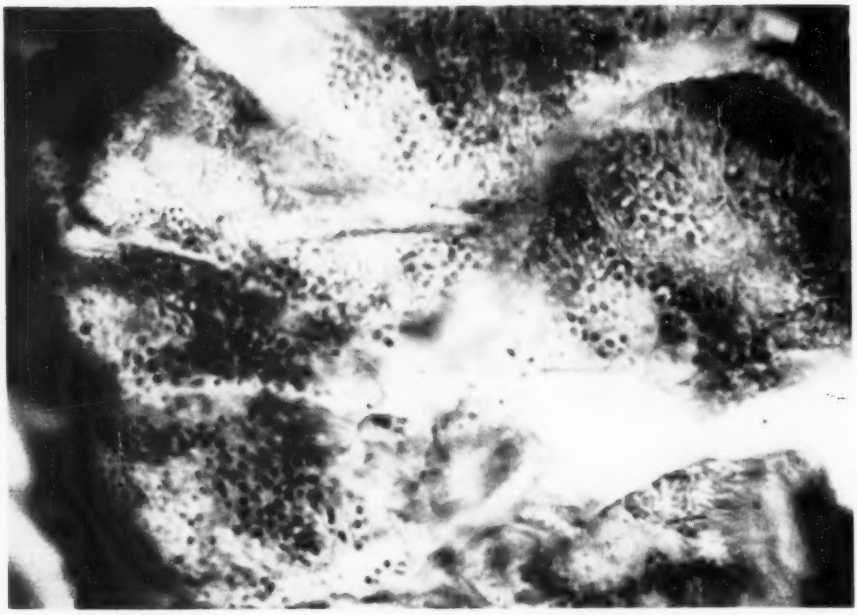

Fig. 3. Detailed view of one of the calcified foci shown in Fig. 2. Note the numerous spherical granules. These stain metachromatic. Toluidine blue. Orig. Mag. 900X.

and at the periphery. On the strip surface and centrally in the plaque they were aligned in perpendicular palisade arrangement, in tuft-like groups, separated by accumulations of cocci. The threads and filaments were also located at the periphery of calcified foci. At the periphery of the plaque the filaments and threads appeared singly and without regular arrangement. It was not possible to distinguish any bacterial structure in the calcified foci within the plaque.

The Cuticle: A homogenous linear cuticular structure ranging from 5 to 50 mu in thickness was observed in 9 out of 60 subjects of the 14 to 70 age group. It was adjacent to the strip and apparently adherent to it. Except in one specimen in which it was present on the third day, the cuticle was not observed until the seventh day or later. The cuticle occurred consistently in specimens from the same individual examined at various intervals. It was not observed in any of the 5 to 12 year old patients.

Roughening of the strip did not affect the incidence of the cuticle formation. However, the inner surface of the cuticle conformed to the indented contours of the roughened strips (Fig. 7).

The cuticle was eosinophilic but did not stain with the other techniques employed in this study. Following hydrolysis with 7 N potassium hydroxide the cuticle stained positive for sulfhydryl groups, suggesting a possible keratinous structure.

Comparison of Plaque Formation on Strips and Adjacent Anterior Teeth. In the 5 to 12 year old group grossly visible plaque was formed on all the strips in all subjects. Clinical examination with explorer at the beginning and termination of the experiment revealed little or no accumulation on the adjacent teeth upon which no strips had been placed. In the 13 to 70 year old group, plaque accumulated upon teeth without strips, as well as upon all the adjacent strip surfaces. However, the amount accumulated on the strips was visibly greater.

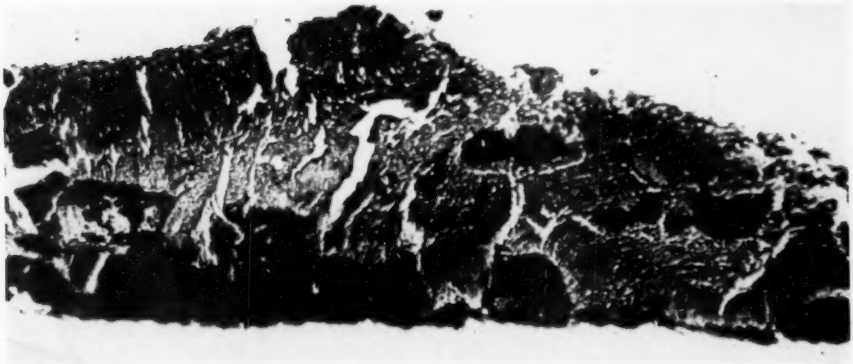

Fig. 4. Serial section of specimen shown in Fig. 2 demonstrating darkly stained calcification foci. von Kossa's silver stain. Orig. Mag. 100X.

DISCUSSION

Our findings are similar to those of previous investigations[1-8] regarding calculus formation on strips attached to teeth in humans in that it starts as a soft adherent mucopolysaccharide plaque which undergoes progressive calcification. Our observations differ from earlier reports in some respects and supplement them in others.

In the non-calcified plaque, in addition to confirming the presence of carbohydrate protein complexes[1-8] we observed protein-bound sulfhydryl, disulfide and amino groups. The significance of the latter groups can only be theorized. They may provide a means for holding the soft plaque together through salt linkages, hydrogen bonding and disulfide linkages, or combine with cationic minerals in the calcification process.

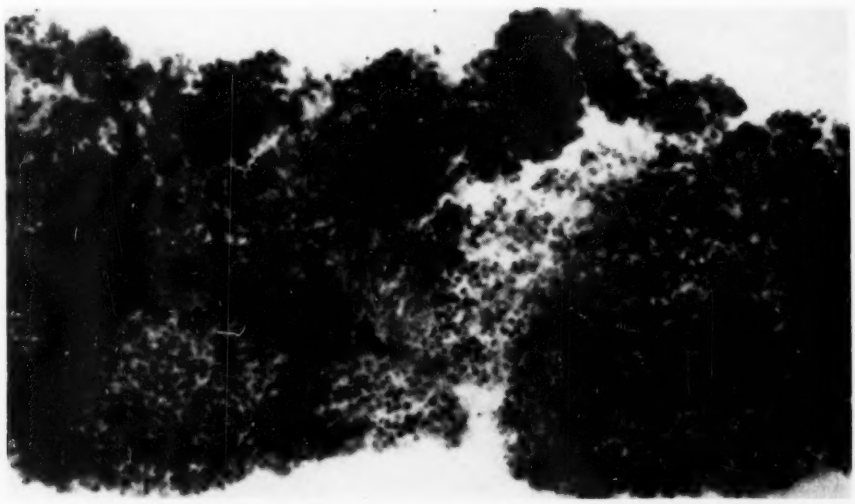

Fig. 5. Three day non-calcified plaque consisting mainly of cocci diffusely distributed and a few rods. Note the ring-like groupings of the bacteria in the lower portion of the plaque. Hematoxylin and Eosin. Orig. Mag. 900X.

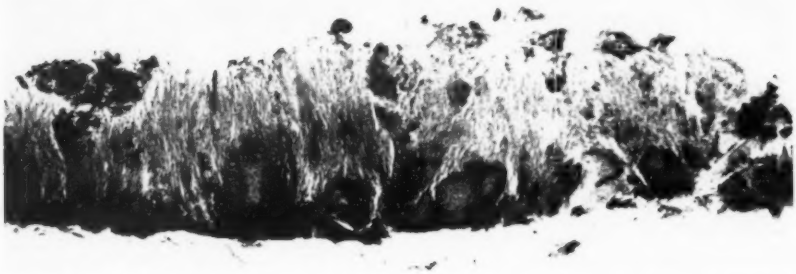

Fig. 6. Five day plaque with areas of calcification showing filamentous and thread forms of bacteria in palisade arrangement perpendicular to the strip surface (lower border). Between the filaments and on the outer plaque surface are colonies of cocci. Hematoxylin and Eosin. Orig. Mag. 100X.

Our findings indicate that Gram negative cocci and rods were predominant in the microbial flora of the non-calcified plaque rather than Gram positive organisms as reported elsewhere.[8] With calcification there was a clumping of these organisms into isolated foci. Filamentous organisms which were rarely seen in the non-calcified plaque increased in number and exceeded the cocci and rods as calcification progressed.

Alterations in the histochemical staining and bacterial flora occurred consistently in plaques which underwent calcification but were not observed in non-calcified plaques. We could not determine whether the alteration in bacterial flora was a necessary preliminary to calcification or whether it was the result of the calcification process.

Several interpretations may be placed upon the histochemical changes which accompanied calcification. It may be assumed that occurrence of metachromasia indicates

Fig. 7. Twenty-four day specimen. The irregular outline of the cuticular structure on the lower border conforms to the roughened strip surface. Hematoxylin and Eosin. Orig. Mag. 900X

a change in the mucopolysaccharides whereby free anionic groups such as sulfates, phosphates or carbonates[9] become available for combination with cationic mineral elements. The increased intensity of the P.A.S. stain at the periphery of the calcification foci and the reduced intensity of the stain within the foci may indicate an increased availability of 1, 2 glycol at the periphery and their reduction after the central portions of the foci have become calcified. The fact that the individual foci increase in size by calcification at the periphery encourages the suspicion that an increased availability of glycol groups is related to the initiation of the calcification process. The staining of the glycol groups in the calcified central portion may be reduced because the glycols are tied to mineral cations or are organically conjugated. We can offer no explanation for the reduction in basophilia which consistently accompanied calcification in our material and has also been described by others.[8]

The histochemical findings referred to above could mean that changes occur in the mucopolysaccharide plaque which prepare it for and precede calcification. This assumption is encouraged by the fact that plaques which do not calcify, do not undergo histochemically detectable changes. On the other hand, we could not establish whether the changes in the mucopolysaccharide plaque actually preceded the calcification process or resulted from it. However, we are inclined to consider the absence of stain with toluidine blue in previously metachromatic areas to be the result of the calcification process. With complete calcification the anionic groups are combined with the mineral cations and are no longer available to the cationic components of the toluidine blue.

It appears quite clear that the local factor is an important determinant of whether and how rapidly calculus formation will occur. When the local environment is changed by wiring a roughened strip to a tooth, calculus forms in a mouth where it ordinarily does not occur. In children with calculus-free natural teeth calculus formed on the strips. In adults who formed calculus on their natural teeth, the strips were the site of increased calculus formation. The rate of calculus accumulation was less on smooth strips than on roughened strips.

Calculus formed in 10 of the 14 subjects in the 5 to 12 year age group. It should be made clear that this occurred on the strips. The natural dentition in these subjects was essentially calculus-free.

The local factor has an important inductive effect upon calculus formation. It leads to accumulation of the soft mucopolysaccharide plaque. Once the soft plaque accumulates it undergoes calcification in the same way in children as it does in adults, but at a slower rate. The local environment is of sufficient significance to induce calculus formation. Apparently other factors in the oral cavity can modify the rate at which calculus accumulates.

We do not know how the calculus is attached to the cellulose acetate strips used in this study. It has been suggested that a cuticle-like substance observed in calculus formed in the mouth on mylar strips attaches the calculus to the strip.[10] We found a cuticle-like substance in only 9 of the 74 experimental subjects. It occurred with equal frequency on smooth and roughened strips.

CONCLUSIONS

Calculus was collected on cellulose acetate strips in seventy four children and adults in the course of a 30 day experimental period.

Bacterial and histochemical features of calculus formation were described.

Calculus formation was induced in calculus-free children by altering the local environment.

Calculus formation on cellulose strips occurs less rapidly in children than in adults, but presents the same histologic and histochemical features.

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The authors acknowledge with thanks the advice and guidance of Dr. Alan Michaels of the Massachusetts Institute of Technology, and the technical assistance of Mrs. Nancy Krasnoo in our laboratory.

A New Adhesive Foil Dressing for Periodontal Surgery

by CHARLES L. BERMAN, D.D.S., FRANK E. BEUBE, D.D.S., RONALD ODRICH, D.D.S., AND AUSTIN H. KUTSCHER, D.D.S., *New York, New York*

PRACTITIONERS who are familiar with the adhesive foil materials currently used in periodontal surgery fully appreciate that those available leave much to be desired in terms both of strength and adhesiveness. The foil often peels from the pack, leaving a dressing which is prone to marginal fracture.

The following is suggested as a method of fabricating a new adhesive surgical dressing with improved qualities.

Rezifilm,* a methacrylate resin, is sprayed on the surface of a large sheet of tinfoil of suitable thickness and allowed to dry. A second coat is then applied. Before the second coat dries, Orahesive** powder is dusted liberally on the surface. When the resin and adhesive are completely dried, the excess powder is removed by inverting and gently shaking the sheet of tinfoil.

Strips of foil are then cut to sizes which are adequate to cover the operative site. The foil is protected from moisture until it is applied to the surface of the wound or placed over a suitable periodontal pack. The foil is gently burnished (without wetting) into all available undercuts.

Preliminary observations with this technique in 40 patients have indicated that such treated foil is highly adhesive, retentive, and protectant. Operative sites have been successfully covered for periods as long as 14 days.

630 West 168th Street, New York 32, New York

The authors express their appreciation for the assistance of Mrs. Helene W. Kutscher and Mrs. Aldonna Skislak, and Audrey Kelley, R.D.N.

Sections of Periodontology and Oral Diagnosis, Division of Stomatology, Columbia University, School of Dental and Oral Surgery, New York, New York.

Orahesive powder and Rezifilm utilized in these studies were supplied through the courtesy of the Squibb Institute for Medical Research, New Brunswick, N. J.

*Rezifilm is a methacrylate resin with tetramethyliuram disulfide, an antibacterial agent, dissolved in ethyl acetate with dichlorodifluoro- and trichloromonofluoromethane as the propellants. The solution is sterile and nonwater-soluble. When sprayed, it rapidly forms a protective film which is flexible, transparent, and non-flammable.

**An adhesive powder composed of a mixture of gelatin, pectin, and carboxymethylcellulose.

The Effect of Anticonvulsant Drugs Upon the Gingiva—
A Series of Analyses of 1048 Patients
II

by HAROLD J. PANUSKA,* ROBERT J. GORLIN,* JACOB E. BEARMAN** AND DAVID F. MITCHELL***

STUDY I. ANTICONVULSANT COMBINED THERAPY AND GINGIVAL HYPERPLASIA

Robinson and Osgood[32] at Mason State Hospital in Massachusetts and Davidson and Sutherland[10] of Glasgow Mental Hospital in England reported that Dilantin and phenobarbital were more successful than Dilantin alone in the control of seizures. One group reported that the expected seizure incidence was reduced eighty-one per cent in their patients.[9] The same logic of combining anticonvulsant drugs has been applied to the new drugs, and at times three and four drugs have been used. Therefore, interpretation of treatment becomes very complex. Rarely did we find a patient on a single drug. In this study there was interest in observing whether these new drugs potentiate or reduce the hyperplasia. Of particular interest was the effect of phenobarbital because of the large amounts given to these patients. Patients were divided into their different drug groups and these were compared with the incidence of hyperplasia in general. No attempt was made to study the drugs in relation to the degree of hyperplasia.

DRUG CALCULATIONS AND CONCLUSIONS

Patients receiving phenobarbital	*N*	*% Hyperplasia*
1. And receiving Dilantin Sodium	474	50
2. And NOT receiving Dilantin Sodium	277	22

k value: 7.45 (probability of exceeding such a k value less than one in a million).

Conclusion: Patients receiving Dilantin and phenobarbital develop hyperplasia more frequently than those receiving phenobarbital alone.

Patients not receiving phenobarbital	*N*	*% Hyperplasia*
1. But receiving Dilantin	69	42
2. And NOT receiving Dilantin	228	10

k value: 6.25 (probability of exceeding such less than one in a million).

Conclusion: Patients receiving Dilantin (and NO phenobarbital) develop hyperplasia more frequently than those not receiving Dilantin (and not receiving phenobarbital).

Patients receiving Dilantin	*N*	*% Hyperplasia*
1. And receiving phenobarbital	474	50
2. And NOT receiving phenobarbital	69	42

k value: 1.17 (this kind of relationship could occur by chance).

Conclusion: Patients receiving Dilantin and phenobarbital develop hyperplasia in nearly the same degree as patients receiving Dilantin alone.

Patients NOT receiving Dilantin	*N*	*% Hyperplasia*
1. But receiving phenobarbital	277	22
2. And NOT receiving phenobarbital	228	10

k value: 3.74 (probability of 2 in 10,000).

DISCUSSION AND CONCLUSIONS

It seems that patients getting only phenobarbital have a higher prevalence of hyperplasia than patients getting neither phenobarbital nor Dilantin; however, it

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Percentage and Number of Patients Displaying Hyperplasia and Receiving the Indicated Drug Combinations

	Phenobarbital		
YES	50% of 474 patients Box C	42% of 69 patients Box B	49% of 543 patients
Dilantin NO	22% of 277 patients Box D	10% of 228 patients Box A	17% of 505 patients
	40% of 751 patients	18% of 297 patients	

will be noticed that the increase in per cent of patients with hyperplasia among patients receiving only phenobarbital (12 percentage points) is much less than the increase over the percentage with hyperplasia among those getting Dilantin as well (28 percentage points).

Note that we still cannot say, in the first case, that phenobarbital, or in the second case, that Dilantin, causes the increase in per cent of patients with hyperplasia. There may be other factors that are *causing* the hyperplasia, e.g., poor oral hygiene leading to local inflammation. All we can say here is that these drugs are associated to a greater or lesser degree with the hyperplasia; no inference is yet to be made concerning specific causation.

For completeness and clarity, note the data presented in a box table for each examination (see table above).

First consider:

1. Box A: 228 patients received neither phenobarbital nor Dilantin; among these 10 per cent showed hyperplasia.

2. Box D: 277 patients received phenobarbital and *No* Dilantin; among these 22 per cent showed hyperplasia.

3. Comparing Box A to Box D, hyperplasia is increased by 12 percentage points among patients on only phenobarbital.

4. Box B: 69 patients received Dilantin and no phenobarbital; among these 42 per cent showed hyperplasia.

5. Comparing Box A to Box B, hyperplasia is increased by 32 percentage points among patients getting only Dilantin sodium.

Next consider these observations:

1. Box C: 474 patients who receive both drugs; among these 50 per cent showed hyperplasia.

2. Box D: 277 patients received phenobarbital and no Dilantin; among these 22 per cent showed hyperplasia.

3. Comparing Box C to Box D, hyperplasia is conversely reduced by 28 percentage points.

4. Box B: 69 patients received Dilantin and *no* phenobarbital; among these 42 per cent showed hyperplasia.

5. Comparing Box B to Box C, hyperplasia is reduced by 8 percentage points.

Conclusion: If one considers what has been said above for only phenobarbital by comparing Boxes B and C (50 to 42 per cent) (eight percentage points difference) with no Dilantin, Boxes D and A (22 to 10 per cent) (12 percentage points difference), it appears that the potentiation factor is of little magnitude and not significant. The small 4 per cent difference could be accounted for by the factor of chance.

If there is some synergism between Dilantin and phenobarbital with regard to hyperplasia, one would expect a greater percentage in Box C than has been observed.

Therefore, from the above data *one can conclude that any hyperplasia that may be associated with phenobarbital alone is masked to a point of insignificance by the Dilantin when both drugs are used in combination.*

The following tabulations are presented to complete the review of ALL the drugs used in any quantity at the institution.

Patients not receiving Mesantoin

No Phenobarbital	*N*	*% Hyperplasia*	*With Phenobarbital*	*N*	*% Hyperplasia*
1. Receiving Dilantin	66	42	1. With Dilantin	469	49
2. Receiving No Dilantin (k value: 7.30)	224	10	2. Without Dilantin (k value: 10.41)	263	22
% difference		32			27

Patients not receiving bromide

No Phenobarbital	*N*	*% Hyperplasia*	*With Phenobarbital*	*N*	*% Hyperplasia*
1. With Dilantin	65	43	1. With Dilantin	456	49
2. Without Dilantin (k value: 6.28)	226	10	2. Without Dilantin (k value: 10.77)	265	22
% difference		33			27

Patients not receiving Mebaral

No Phenobarbital	*N*	*% Hyperplasia*	*With Phenobarbital*	*N*	*% Hyperplasia*
1. With Dilantin	34	47	1. With Dilantin	412	49
2. Without Dilantin (k value: 5.87)	218	9	2. Without Dilantin (k value: 10.80)	259	21
% difference		38			28

Patients not receiving Hibicon

No Phenobarbital	*N*	*% Hyperplasia*	*With Phenobarbital*	*N*	*% Hyperplasia*
1. With Dilantin	66	44	1. With Dilantin	469	49
2. Without Dilantin (k value: 6.48)	228	10	2. Without Dilantin (k value: 10.94)	276	22
% difference		34			27

Patients not receiving Miscellaneous Drugs (Including Tridione)

No Phenobarbital	*N*	*% Hyperplasia*	*With Phenobarbital*	*N*	*% Hyperplasia*
1. Receiving Dilantin	68	43	1. With Dilantin	454	49
2. Without Dilantin (k value: 6.40)	225	9	2. Without Dilantin (k value: 11.09)	271	21
% difference		34			28

In the above five tabulations, the single drug has been eliminated with the hope of testing to see if any potentiating effects were present. These may be summarized by placing the percentage *differences* (the differences in percentage of hyperplasia between those patients receiving Dilantin and those not receiving Dilantin) below. Thus, they can be easily compared:

Drug Eliminated	*Percentage difference of hyperplasia between those getting Dilantin and those not getting Dilantin sodium*	
	No Phenobarbital	*With Phenobarbital*
None (all patients)	32%	28%
1. Mesantoin	32	27
2. Bromides	33	27
3. Mebaral	38	28
4. Hibicon	34	27
5. Miscellaneous	34	28

The differences, when each drug is eliminated in turn are in agreement with the differences when all patients are concerned, i.e., no drugs eliminated. This seems to indicate that in this group of patients, eliminating mesantoin, bromides, Mebaral, et cetera, individually, seems to have no effect on the Diltantin-no Dilantin percentage of patients with hyperplasia, both in the presence of or in the absence of phenobarbital.

In conclusion, this would further indicate that any potentiating effect of these drugs, if present, is not discernible from these data.

STUDY II. RELATIONSHIP OF ORAL HYGIENE TO HYPERPLASIA

Poor oral hygiene has been stated to be associated with Dilantin hyperplasia by Ziskin, et al,[42] Staple,[37] and Stern, et al.[38] However, it was noticed by Glickman and Lavitus[18] that the hyperplasia occurred in both clean and dirty mouths. They further stated that some patients with heavy deposits of calculus show no hyperplasia while others with good oral hygiene may show extreme hyperplasia. They did not seem convinced of the importance of local irritants. Millhon and Osterberg[27] and Esterberg and White[13] also found no relationship of oral hygiene to the incidence of hyperplasia.

In this series, the oral hygiene, as previously stated, was rated by values I through V, class I denoting the best and class V the poorest oral hygiene. In this phase, the hyperplasia ratings given previously to each of the six areas of the mouth were added together and will be referred to as the *"Hyperplasia Index."* These indices range from one to tweny-four. The joint frequency distribution of oral hygiene ratings and hyperplasia indices are given below.

From these data, a chi-square (with 24 degrees of freedom) value of 71.77 was calculated. This calculation was performed after grouping hyperplasia index numbers (next table) as follows: for each of five oral hygiene classes, Hyperplasia Index class zero and one were combined for group I; Hyperplasia Index class two, three and four were combined for group II; five, six and seven for group III; classes eight, nine and ten into group IV; eleven, twelve and thirteen into group V; fourteen, fifteen and sixteen into group VI; and seventeen through twenty-four making group VII,

Oral Hygiene Classes 1043

Hyperplasia Index	*I*	*II*	*III*	*IV*	*V*
0	237	126	123	103	110
1	11	13	14	7	2
2	15	15	2	8	2
3	4	18	8	3	5
4	10	8	12	4	4
5	3	10	8	5	1
6	0	5	4	4	6
7	1	2	4	2	5
8	3	5	5	2	3
9	4	4	3	3	2
10	0	1	2	2	2
11	1	4	1	0	3
12	0	5	2	3	1
13	0	0	3	1	0
14	0	2	2	2	2
15	0	3	3	3	3
16	1	0	2	2	3
17	0	0	1	1	0
18	0	0	0	3	1
19	0	2	2	1	1
20	0	2	1	1	1
21	0	0	2	0	3
22	1	0	0	0	0
23	0	0	1	0	1
24	0	0	0	0	1
Total	291	225	205	160	162

Chi-square = 71.77

thus a total of seven Hyperplasia Index class groups. The purpose of making the seven class groups from the original twenty-four was to give a reasonably large number of cases in the extremities where the observed values were small. By doing this, the observed values more closely approximate the minimum acceptable expected values of five in each cell for performing the chi-square tests. Several further telescopings of the hyperplasia classes were done. For example, groups V through VIII, which actually consist of original classes eleven through twenty-four, were combined and the chi-square value of 65.94 calculated. This was done to obtain the most conservative possible evidence concerning the distribution of the hyperplasia index in the various oral hygiene classes. All such calculations indicated that the different oral hygiene classes exhibit *different* frequency distribution of Hyperplasia Index.

Thus, it can be concluded, until further evidence to the contrary appears, that there is a difference in the distribution of Hyperplasia Index among oral hygiene classes.

A further test was applied to the data because of a belief that class I oral hygiene was the largest contributor to the chi-square and because we wanted to see it, with the elimination of clean mouths, there was a difference among the other groups (two through five) when applying the same test.

Class intervals of Hyperplasia Index	*Oral hygiene classes* 2	3	4	5
I	139	137	110	112
II	41	22	15	11
III	17	16	11	12
IV	10	10	7	7
V	9	6	4	4
VI	5	7	7	8
VII and VIII	4	7	6	8

From the above, a chi-square value of 19.5 was calculated (this table has eighteen degrees of freedom) having an associated probability value of one-third, indicating very little reason for suspecting that oral hygiene groups two through five are really different from each other in Hyperplasia Index distribution.

In conclusion, from these data we find that class I oral hygiene is different from classes II through V with respect to hyperplasia distribution. Next, a comparison of class I and classes II through V is made.

A Comparison of Classes II-V with Class I

	Oral Hygiene Classes *Class I*	*Classes II-V*	*Totals*
1	248	498	746
2	29	89	118
3	4	56	60
4	7	34	41
5	1	23	24
6	1	27	28
7 & 8	1	25	26
	291	752	1043

The Hyperplasia Index classes are combined in the same way as previously presented. The chi-square value (with six degrees of freedom) for the above table is 49.5 (this has a probability value of less than .0005). Thus, *it may be concluded that patients with poor oral hygiene have more hyperplasia than those with good oral hygiene.* We have not been able to perform any test to examine whether there is *increased* Hyperplasia Index (in the II through V group) associated with increasingly poor oral hygiene. These observations do not mean poor oral hygiene causes hyperplasia, it only means poor oral hygiene is *associated* with hyperplasia. In fact, the converse may well be true, i.e., that the hyperplasia may be the cause of the poor oral hygiene.

The 1043 patients analyzed above were next divided into two groups: (a) those receiving Dilantin and those not receiving Dilantin. The *No* Dilantin group consisted of 504 patients and the *Yes* Dilantin group of 539 patients.

In the *No* Dilantin group the chi-square (based on 24 degrees of freedom) is 24.35. Notice the marked contrast to the value

Oral Hygiene Classes and Hyperplasia Index—*No* Dilantin and Dilantin
TOTAL = 1043

	No Dilantin (N-504)					*Yes Dilantin* (N-539)				
	1	2	3	*4*	5	*1*	2	3	*4*	5
0	121	76	78	72	75	116	50	45	31	35
1	3	8	4	4	0	8	5	10	3	2
2	2	4	1	4	0	13	11	1	4	2
3	1	4	4	0	1	3	14	4	3	4
4	1	2	2	1	3	9	6	10	3	1
5	1	2	1	2	1	2	8	7	3	0
6					1		5	4	4	5
7					2	1	2	4	2	3
8	3	2	1		1		3	4	2	2
9	1	1	2	2	1	3	3	1	1	1
10							1	2	2	2
11	1				3		4	1		
12							5	2	3	1
13			1					2	1	
14							2	2	2	2
15				1	1		3	3	2	2
16						1		2	2	3
17								1	1	
18									3	1
19					1		2	2	1	
20							2	1	1	1
21								2		3
22	1									
23								1		1
24										1
	135	99	94	86	90	156	126	111	74	72
	Chi-square = 24.35					Chi-square = 85.17				

previously obtained. This is interpreted to be a chi-square that is accounted for almost perfectly by chance alone and means that there is no evidence for suspecting any real difference in oral hygiene classes I through V.

In the *Yes* Dilantin group the results were similar to those found previously. The chi-square in the *Yes* group is 85.17.

This is conclusive enough to say that there is a definite relationship of the oral hygiene and the Hyperplasia Index among patients treated with Dilantin. Note that this is in marked contrast with the patients not currently under Dilantin treatment.

While it appears that there is no association between oral hygiene and Hyperplasia Index when patients are not on Dilantin, there is a clear cut difference in hyperplasia distribution when patients are on this drug. This would indicate that there is some relationship (unknown as yet) among Dilantin, oral hygiene, and hyperplasia. Possibly some interaction has taken place or there is a synergistic effect somewhere among them. It should be noted that in the *Yes* Dilantin group (presented above) the same type of relationship exists as did in the previous study of the entire group. That is, the oral hygiene in group I differs markedly from the II through V groups. A chi-square value (based on 18 degrees of freedom) of 18.90 was calculated from the *Yes* Dilantin table for this latter group. This indicates as before that there is no real difference among the groups. (Compared with chi-square value of 19.5 for similar calculations done on the entire 1043 patients previously). The difference in distribution is therefore clear cut between group I and the combined groups II through V. Thus, any difference observed previously seems to be accounted for by those patients under Dilantin treatment.

STUDY III. YEARS OF MEDICATION AND DEGREE OF HYPERPLASIA

The length of time patients have been taking Dilantin sodium and the amount of hyperplasia they have experienced has received some attention in the literature. The minimum time limit under Dilantin treatment before the appearance of symptoms has been suggested by Jurgens[21] and Staple[37] as two weeks, but they noted further that it is usually a matter of several months. Kimball[22] reported changes in sixty-eight patients under Dilantin therapy, fifty-seven per cent showing changes in two or more months. Some of Kimball's patients, however, went eleven months without any visible change. Dummett[11] and Orban and Wentz[28] claimed it occurs in about three months.

In this survey we did not study the length of time before onset; most of our patients being chronic users of Dilantin. We did, however, record the number of years patients received medication. According to Burket[7] the degree of hyperplasia is not related to the dosage or length of administration of the drug, although there seems to be a tendency for the gingival changes to occur in individuals receiving larger doses for some length of time. Stern, Eisenbud, and Klatell[38] suggested a correlation between the severity of the lesion and the duration of drug therapy. Esterberg and White[13] found no correlation between duration of drug therapy and degree of hyperplasia. Ziskin, Stowe, and Zegarelli[42] did not find a correlation with time but suggested it might be a factor. Esterberg and White[13] found that a quick increase in dosage precipitated gingival hyperplasia in patients under therapy without previous signs of gingival change. One of the authors has observed two cases in which sharp increase in dosage has precipitated the hyperplasia and subsequent retraction of the drug did not decrease the hyperplasia.

In our group of 1048 patients, the Hyperplasia Index was used and individual cases were separated into groups according to "years under medication." Because of the small number of cases in each cell, and in order to facilitate calculations, the Hyperplasia Indices were grouped as previously discussed in the section on Oral Hygiene. Years were grouped as follows: 1-5, 6-10, 11-15, 16-20, and each of these four groups was divided into those currently receiving Dilantin and those not currently receiving Dilantin, realizing of course that the group not currently receiving Dilantin might contain some patients who had received Dilantin previously. This we did not feel seriously affected our results, for if we did see a difference, those patients would only have tended to obscure it.

Within each of these groups the distributions of patients by Hyperplasia Index were compared. For example in the 1-5 years on medication group, the distribution of patient Hyperplasia Index in the group *not* currently under Dilantin treatment was compared with the distribution of Hyperplasia Index of those patients who *were* currently under Dilantin therapy, similarly in the 6-10, 11-15, and 16-20 groups. The results of these comparisons are shown in the table on the following page.

It should be readily observed from the above table that the probability values ($p\ X^2_6$) become increasingly smaller as the length of time increases. This means that the actual difference of the patients that are currently on Dilantin and those not currently on Dilantin treatment becomes more significant as the years of medication increase. It may now be inferred from these values that a patient on Dilantin shows an increasing relationship between the amount of hyperplasia and the length of time on medication. The probability value of the less than 1 to 5 year group is .174; this value would give us little reason to suspect a difference in the two groups. In the middle two five-year periods the values .020 and .043 are essentially of the same magnitude and indicate a reason for suspecting a difference even though this difference is of minor signifi-

Years Under Medication and Hyperplasia Index

	1-5		6-10		11-15		16-20	
Hyperplasia Index	*No Dil.*	*Yes Dil.*	*No Dil.*	*Yes Dil.*	*No Dil.*	*Yes Dil.*	*No Dil.*	*Yes Dil.*
0- 1	43	53	33	44	43	57	113	127
2- 4	5	18	2	15	6	14	6	29
7- 7	1	9	2	8	2	14	2	18
8-10	4	9	2	4	2	8	3	5
11-13	2	4	1	5	0	2	2	6
14-16	2	7	0	8	0	2	0	7
17-24	1	3	0	5	0	6	1	10
Totals	58	103	40	89	53	103	127	202
C(O-e) 2/e=	9.24		15.20		13.02		29.95	
P X^2_6 =	.174		.020		.043		.0005	

cance. In the 16-20 year group the value of .0005 is obviously very strong evidence that the groups are significantly different. This evidence seems to indicate that the difference which is expressed by the probability value obtained from the data above becomes more apparent as time increases. Patients under current Dilantin treatment show more hyperplasia as medication time is increased. Because of the incompleteness of records at the hospital, we were not sure whether these patients were under Dilantin treatment for the full time of their medication period, but it was assumed that they may have been and interpretation of these data must take this into account.

Thus far, then, with an increased number of years under medication, there is increasingly more reason to suspect a real difference in distribution of Hyperplasia Index between currently Dilantin treated patients and those not currently on Dilantin. But a closer look at the number of patients involved in the individual groups led us to examine further the data. The number of patients in the 16-20 year group is materially larger than the other two or three. With this in mind we were concerned that the apparent significance might be reflecting merely the larger sample size which is so apparent in the 16-20 year group. To explore this possibility further we combined groups 1-5, 6-10, and 11-15 to obtain a total number of individuals somewhat larger than the original 16-20 group of 329 patients. This new group totaled 446 patients, a much more even comparative group than previously examined. See below:

Table of Combined Group (1-15 Years) and the 16-20 Group

		1-15 Years	
Hyperplasia Index		*No Dilantin*	*Yes Dilantin*
0- 1		119	154
2- 4		13	47
5- 7		5	31
8-10		8	21
11-13		3	11
14-16		2	17
17-24		1	14
E (c-e) 2/3	=	151	295
		32.97	
P X^2_6	=	.0005	

Examination of these data indicated that this probability value is of the same magnitude as that previously observed for the 16-20 year group in the first table. Hence, it is not clear that length of time under medication is the effect we are observing in these data. But perhaps we only see the reflection of the difference in the sample size observed in the years of treatment group.

STUDY IV. SEX AND HYPERPLASIA

A review of the literature reveals that the influence of sex upon the incidence of Dilantin hyperplasia is practically nil. Ishikawa[20] reported a hyperplasia incidence of 57 per cent in males and 55 per cent in females. Our series was investigated with the hope of giving some statistical evidence of the relationship, be it positive or negative.

The 1048 patients were divided according to sex into 489 males and 559 females. The same hyperplasia index was used as before in STUDY II AND STUDY III, and a similar grouping of the indices was employed. No attempt was made to separate Dilantin from *No* Dilantin patients at first inspection:

Sex and Hyperplasia Index

Hyperplasia Index	*0–1*	*2–4*	*5–7*	*8–10*	*11–13*	*14–16*	*17–24*	*Total*
Males	311	68	34	23	17	17	19	489
Females	439	50	27	18	7	11	7	559

A chi-square value was calculated for the above equal to 32.47, with an associated probability value of less than .0005. This value indicated there was a definite difference in the above distributions. A further investigation of the material was then done. First, the patients were divided into those *not* receiving Dilantin and those receiving Dilantin. The males and females were distributed as shown by the Hyperplasia Index.

Sex and Hyperplasia-*No* Dilantin

Hyperplasia Index	*0–1*	*2–4*	*5–7*	*8–10*	*11–13*	*14–16*	*17–24*	*Total*
Males	172	19	4	9	3	1	1	209
Females	271	11	6	5	2	1	1	297

A chi-square value from the figures in the above table (*No* Dilantin group) is equal to 10.96 and the associated probability value of .09 which is questionable evidence of a difference in distribution of the Hyperplasia Index between males and females when *not* under Dilantin Treatment.

Sex and Hyperplasia Under Dilantin Treatment

Hyperplasia Index	*0–1*	*2–4*	*5–7*	*8–10*	*11–13*	*14–16*	*17–24*	*Total*
Males	139	49	30	14	14	16	18	280
Females	168	39	21	13	5	10	6	262

A chi-square value of 16.63 and an associate probability value of .009 was calculated from the above table (those receiving Dilantin). This is considered good evidence of there being a difference of Hyperplasia Index distribution between the males and females when they receive the drug. Thus, it seems that the difference between hyperplasia distribution of males and females found in the first table is contributed primarily by patients under Dilantin treatment.

The same data from these last two tabulations are presented as a percentage frequency distribution below, because of the fact that the chi-square does not lend itself to the interpretation of location.

In presenting the percentage distribution, it should be observed that for both males and females in the *Yes* Dilantin group the percentage in the *No* hyperplasia group (0-1) is diminished and in *every* other case or category of hyperplasia *there is an increase in the percentage of patients with hyperplasia* over the corresponding category in the *No* Dilantin group.

Percentage Frequency Distribution—*No* Dilantin

Hyperplasia Index	*0-1*	*2-4*	*5-7*	*8-10*	*11-13*	*14-16*	*17-24*
Males	82.30	9.09	1.91	4.31	1.44	.48	.48
Females	91.25	3.70	2.02	1.68	.67	.34	.34

Percentage Frequency Distribution—*Yes* Dilantin

Hyperplasia Index	*0-1*	*2-4*	*5-7*	*8-10*	*11-13*	*14-16*	*17-24*
Males	49.64	17.50	10.71	5.0	5.0	5.71	6.43
Females	64.12	14.89	8.02	4.96	1.91	3.82	2.29

It is now interesting to look at the intra sex differences between Dilantin and *No* Dilantin patients. Note that among the *Yes* Dilantin-*No* Dilantin patients the chi-square value and associated probability are almost identical for males and females. Thus, the evidence seems to indicate that Dilantin is associated with similar effects on both sexes as measured by chi-square. Furthermore, the difference between Dilantin and No Dilantin for each sex is much more strongly indicated than between sex differences.

Nevertheless, examination of the data above (Percentage Frequency Distribution-*No* Dilantin) seems to indicate that the males have a smaller percentage with no hyperplasia than the females, and a larger percentage in every category of hyperplasia than do the females. The same trend, but

Females

Hyperplasia Index	*0-1*	*2-4*	*5-7*	*8-10*	*11-13*	*14-16*	*17-24*	*Total*
Yes Dilantin	168	39	21	13	5	10	6	262
No Dilantin	271	11	6	5	2	1	1	297

Chi-square equals 61.82 Probability value equals less than .0005

Males

Hyperplasia Index	*0-1*	*2-4*	*5-7*	*8-10*	*11-13*	*14-16*	*17-24*	*Total*
Yes Dilantin	139	49	30	14	14	16	18	280
No Dilantin	172	19	4	9	3	1	1	209

Chi-square equals 64.29 Probability value equals less than .0005

certainly to a lesser degree, seems to appear in the table, Percentage Frequency Distribution-*Yes* Dilantin. What this means is not clear; it may be reflecting such things as more attention to better oral habits among women, i.e., the female consciousness of personal appearance, and attempts to "do something" to counteract the development of unsightly hyperplasia.

STUDY V. RACE AND HYPERPLASIA

As was mentioned previously, the patients were divided by race into three categories: white, negro, and other. The assembled data revealed that it was impossible to interpret any racial difference. There were simply not enough cases of non-whites to warrant further study in this area. Dummett[11] reported no racial difference in his study.

STUDY VI. HYPERPLASIA INDEX AND DAILY DOSAGE OF DILANTIN SODIUM

There are several conflicting reports in the literature concerning the relationship of increased dosage of Dilantin and increased degree of hyperplasia. Esterberg and White[13] reported no relationship between the amount of Dilantin taken and number of severe oral lesions. Stern, Eisenbud and Klatell[38] also report no relationship to increased dosage. Ishikawa[20] reported contrary evidence and stated that there seemed to be some relationship to both drug duration and the daily dosage. Ziskin, Stowe and Zegarelli,[42] on the other hand, reported no association and supported the assumptions and findings of the first two papers. Millhon and Osterberg[27] reported no correlation of amount and degree of hyperplasia with dosage.

The daily dosage of Dilantin was recorded from hospital records, and during the observations of the patients' mouths this information was not available to prejudice the observer.

The original data from which the following summary figures were derived, were analyzed by the technique of analysis of variance recognizing the shortcomings of this method with data such as these. The F-Ratio determined has an associated probability of less than one per cent. This small probability would be good evidence that the differences in the Hyperplasia Index observed could hardly be attributed to the factor of chance. Indeed, it would be taken as strong evidence of increased Hyperplasia Index being associated with an increased daily intake of Dilantin; however, the data are not of a kind to have the analysis of variance best applied to them. This was done merely to obtain some suggestions of relationship between Hyperplasia Index and daily intake of Dilantin. Thus, these results must be interpreted as only suggestive and not as definitive.

Summary of Data

	Dilantin grains per day		
	1 and 2	*3 and 4*	*5 and 6*
Average Hyperplasia Index	2.95	3.17	4.50
Number of People Totals	177	180	183

STUDY VII. EXCESSIVE BODY HAIR AND DILANTIN THERAPY

Reyes[31] and Esterberg and White[13] observed several cases of excessive body hair growth in patients under Dilantin therapy. The faces and limbs of our patients were examined. The cottage aides who were well acquainted with the daily care of these

patients were present to give any information about shaving the patients, and their impressions of excess hair growth. Because of the marked variation in the range of normal hair in males it was decided to eliminate them from the study and to concentrate on the females. The table below shows the abstracted data.

Hirsutism

	Excess Hair	*Normal*	*Total*
No Dilantin	56	241	297
Yes Dilantin	54	207	261
Total Females	110	448	558

The above series includes all of the females in the study. A chi-square value of 27.51 was calculated, equal to a value of less than one. This test provides no evidence for concluding from these data that any difference exists in the occurrence of excess body hair in patients on Dilantin therapy over those not on Dilantin therapy. Thus, this series of patients provides no corroborative evidence for the suggestion that the occurrence of excess body hair is associated with the drug therapy.

STUDY VIII. DILANTIN HYPERPLASIA AND SPECIFIC AREAS OF THE MOUTH

For this study, the mouth was divided into six areas previously illustrated in Figure 3. Hyperplasia was graded I through IV as previously discussed and illustrated in Figures 4-9. The definitions of the four grades of hyperplasia were given by Harris and Ewalt.[19] Several references have been made to specific oral areas of Dilantin hyperplasia. Millhon and Osterberg,[27] Esterberg and White,[13] and Gable[16] all noted hyperplasia to be most prominent in the anterior region. Reyes[31] and Brandon,[6] however, suggested areas of salivary contact as a frequent site, e.g., the upper posterior area. To examine these possibilities more closely three charts were made and the areas were plotted as individual cases against each other. Each diagram included a total of 546 patients, all of whom were taking Dilantin. A relative prevalence could be computed for each area, as presented below:

Prevalence of Dilantin Hyperplasia

Right Posterior	30.71%
Left Posterior	31.70%
Anteriors	46.39%
Average	36.23%

From this we may conclude, as previously suggested by other authors, that the anterior regions have a greater prevalence than posterior regions. In fact, the per cent prevalence in the anterior is significantly different from the percent difference in the posterior with a probability value of less than .01.

To investigate the posterior areas individually, the cases were divided according to: (1) whether they favored higher prevalence in the specific area, or (2) whether they had no apparent effect. The anterior regions were similarly divided.

From the "Summary of Percentages" below, it can be concluded that the hyperplasia is 3 to 4 times more prominent in the upper posterior than in the lower posterior regions. In the anterior regions the mandible is slightly favored but the difference is small. Perhaps it was from these types of data that others drew their conclusions concerning areas of salivary contact. From these data it appears there are some influencing factors which seem to promote the hyperplasia in these specific areas. Whether these are related to salivary flow or to poor cleansing remains to be investigated.

Summary of Percentages

Area (region)	*Favoring Upper*	*Favoring Lower*
Right Posterior	20.88%	7.12%
Left Posterior	20.52%	5.32%
Anteriors	16.12%	18.14%

By applying the chi-square test to the data, it was found that the upper and lower quadrants are dependent, i.e., if hyperplasia was present in the upper, then such patients will have, more likely than not, hyperplasia in the lower; or, these quadrants are not independent of hyperplasia prevalence. It is also noted that if the degree of hyperplasia is high in one quadrant, it is more likely to be high in other areas of the same mouth.

SUMMARY AND CONCLUSIONS

After several attempts to produce hyperplasia in laboratory animals had failed, it was decided to perform a series of studies at the state hospital for epileptics and learn as much as possible by epidemiological methods about drug induced gingival hyperplasia. The methods used and the techniques employed were kept simple. Each patient was examined in his cottage and the information was recorded on forms which would facilitate easy transfer to IBM cards. The IBM was used because of the large number of patients (1048) and the amount of information to be extracted.

1. Patients receiving phenobarbital without Dilantin have a higher prevalence of hyperplasia than those patients receiving no drugs. (These patients were receiving no other drug at the time, and to the best of our knowledge only phenobarbital.) This may lead to the supposition that phenobarbital is associated with hyperplasia also, only to a lesser degree. This may well be true, but we cannot be sure that some of these patients did not receive Dilantin in the past, and that the medication was changed—possibly because of the hyperplasia itself.

2. Any hyperplasia associated with phenobarbital alone was found to be masked to a point of insignificance by the Dilantin hyperplasia when both drugs were used in combination.

3. Patients being treated with Mesantoin, bromides, Mebaral, Hibicon, and Tridione were eliminated one at a time from the total number of patients on combination of drugs, particularly Dilantin. We could not see any potentiation of the hyperplasia or reduction of same by these other drugs. The only conclusion we could draw is that the potentiation or reduction effects of each of these drugs if present are not discernible in these data.

4. The testing of oral hygiene and its relationship with a Hyperplasia Index first led us to the conclusion that there was no association between the two when the patients were not on Dilantin. However, there is a clear-cut difference in hyperplasia distribution when patients are on Dilantin. Thus, there seems to be some relationship among Dilantin, poor oral hygiene, and hyperplasia. What this is, we are not prepared to say. It may involve the extrinsic influences of inflammation, irritation or some unknown factors.

5. The length of time patients take Dilantin appeared at first to be correlated with the amount of hyperplasia. Further examination of the data, however, and attempts to equalize sample size, led us to the final conclusion that the evidence is not clear-cut and that no correlation was discernible from these data.

6. Dilantin has similar effects on both sexes, but hyperplasia seems to exhibit a small degree of preference for males in our study. This may mean that the androgens have some relation to this problem, or perhaps the estrogens display some protective mechanism. These hints are all that were hoped for in this survey.

7. We did not have enough non-white cases to draw any conclusions concerning race and hyperplasia.

8. The observation of Reyes and Esterberg about excessive body hair could not be substantiated. No corroborative evi-

dence of any difference between the Dilantin and the *No* Dilantin groups of patients and the associated amount of body hair could be found. There were as many patients with hirsutism taking Dilantin as there were without it. It might be suggested that some other associated hormonal imbalance could be presented in epileptic patients but that Dilantin does not appear to have any relationship.

9. There is a suggestion of positive correlation between the amount of daily intake of Dilantin and the increased Hyperplasia Index. The greater the daily dosage the more severe the hyperplasia. This is merely a suggested conclusion, and the question requires further investigation in order to be conclusive.

10. A study of the specific areas of the mouth showing hyperplasia seemed to agree with other authors' observations. There seems to be a higher prevalence in the anterior than in the posterior regions. However, our study also showed that the upper posterior showed more hyperplasia than the lower posterior regions. There was very little difference between the upper and lower anterior areas. The suggestion that hyperplasia is greater in areas of salivary contact seems not inconsistent with the present data and should be investigated further regarding the mechanism of action.

Roger E. Huntington, D.D.S.

December 18, 1960

The good friend and inspiration to so many Academy members, Roger E. Huntington, passed away after an illness of several months in Evanston Hospital last December the Eighteenth.

Dr. Huntington graduated from Northwestern and practiced in Evanston from the year of his graduation in 1911 to 1945 when a slight stroke made it impossible to continue longer.

Roger was a member of many organizations but the American Academy of Periodontology, its aims and activities, was always first in his dynamic and energetic mind. It was impossible to be with him long without becoming infected with his enthusiasm. His intolerance for imperfection in practice and thought was occasionally merciless but no one of us who came under his spell could ever again be the careless and inefficient operators that we were.

Roger never influenced large groups directly, but in small "jam" sessions and study clubs he was the master. His physical handicap did not stop or discourage him and in fact it gave him the opportunity to attend more meetings and to encourage and stimulate more interest in periodontia.

To those who knew him well he will be missed but never forgotten; Roger Huntington has my nomination as the most unforgettable character I have ever known.

Randall L. Wescott, 636 Church Street, Evanston, Illinois

Correlation of Blood Constituents with Periodontal Disease
1. Acetylating Activity

by A. C. Hue, D. Y. Burrill, L. S. Fosdick, *Chicago, Illinois*

IT is generally believed that periodontal disease is caused by a combination of local and systemic disturbances.[1,2] The local factors which may lead to oral irritation such as microbial infection, calculus and occlusal trauma have been rather intensively studied. The non-local factors have been attributed to dietary deficiencies and hormonal or metabolic imbalance,[3,4,5] but as yet there seems to be no clear-cut relationship established. In most instances the disease may be kept under control by local treatment, but in some cases the non-local factors are apparently of such intensity that local treatment will not suffice. A number of individuals have produced changes, similar to those that occur in periodontal disease in animals by producing dietary deficiencies.[6,7,8]

Glickman found that a type of osteoporosis could be induced in mice by the administration of Cortisone.[9] The symptoms could be relieved by the use of estrogens.[10]

Although periodontal disturbances can be produced in animals the evidence that vitamin deficiencies and hormonal and nutritional disturbances play specific roles in the disease in man is not clear. Vitamin therapy per se does not effect a cure although in some cases it may accelerate healing.

In 1955 Becks[11] found the blood levels of pantothenic acid lower in individuals suffering from periodontosis and periodontitis. He further found that after a given dose of niacin, people with normal periodontal structures excreted more of the given dose than did periodontal cases.

Karshan[12] found a higher alkaline phosphatase activity in the gingival blood of periodontal cases than in gingival blood from normal cases. Thus, although there is considerable evidence that nutritional and systemic conditions may play a role in periodontal disease, only niacin, pantothenic alkaline and phosphatase have been definitely implicated. There is circumstantial evidence that the entire Vitamin B complex, Vitamin C, possibly Vitamin A, insulin, and the ketosteroids of the adrenals may be involved.[5]

One reaction that is involved in carbohydrate, fat and protein metabolism as well as the synthesis of steroids is that of the transfer of acetyl groups. This is also involved in the synthesis of acetyl choline and in the detoxication of many toxic substances. The transfer of acetyl groups either for the synthesis of specific compounds, or during the catabolic and anabolic reaction of steroids, carbohydrate, fat and protein, requires a number of the members of the Vitamin B complex. In addition to the specific enzyme, CoASH, a derivative of pantothenic acid is always required. Furthermore, a source of acetyl groups is also required.

Acetylation, one reaction associated with the transfer of acetyl groups, particularly in regard to detoxication has been studied for many years.[13,14,15] Most of the work has been accomplished by feeding experiments in which the acetylated compounds were isolated and identified in the urine. Later it was shown that most of these reactions were localized in the liver. Klein and Harris[16] reported that the blood was devoid of acetylating activity. However, Zebaldi[17] found that partial hepatectomy did not materially decrease acetylating activity. Goldberg[18] suggested that the blood

This study was supported by a United States Public Health Grant, No. D-395 in the Chemistry Department, Northwestern University Dental School Clinics and Laboratories.

The report is from a dissertation submitted to the faculty of the Graduate School of Northwestern University by A. C. Hue in partial fulfilment of the requirements of the degree of Doctor of Philosophy.

did contain an acetylase which could acetylate the free amino group of procaine. It was not until 1955 that the acetylating activity of blood was definitely established and a method devised which would accurately detect this activity.[19] Blondheim showed that para-aminobenzoic acid (PABA), when introduced into blood in vitro, became acetylated. His method of detection was based upon the disappearance of PABA when incubated in blood. He found that the disappearance of PABA was increased in the presence of glucose and was inhibited by the presence of fluorides. He found that the enzyme acetylase was concentrated in the formed elements of the blood, but that the plasma was essential as a source of the acetyl group.

It was thought that a comparison of acetylating activity of whole blood from normal and periodontal patients may be of interest. Even though the procedure did not specifically determine acetylase activity, it did determine a complex—many variables of which have been previously implicated in periodontal disease. Before the comparison was made, however, it was thought that the work of Blondheim should be checked in order to make sure that the disappearance of the PABA acid would measure acetylating activity. This was done and in addition the acetylated PABA was isolated and identified by paper chromatographic methods.

PROCEDURE

Subjects were selected from those applying to the Clinic for service. Only those individuals who presented clinical and radiographic symptoms of advanced periodontal disease, seemingly excessive for the apparent local causes, and those whose gingival conditions were normal, were used in this study. Complete mouth examinations, including radiographs were taken, and if selected for the experiment a sample of blood was obtained and sent to the Department of Chemistry for analysis. After one hundred cases of normal and periodontal diseases were obtained, the clinical data was oriented with the chemical data. The acetylating activity of the blood was measured by means of the Blondheim technique using 5 ml. of heparinized whole blood. Check analyses were made on each sample of blood.

Five ml. of heparinized whole blood was pipetted into a sterile centrifuge tube and 0.2 ml. of 3.6 mM PABA solution was added to it. The tube was stoppered and the contents were mixed well. After pipetting 1.0 ml. for the estimation of the initial PABA concentration into a centrifuge tube, the rest of the blood was incubated at 37°C. for 24 hours. The mixture was shaken several times during the incubation period. At the end of the incubation period, the final PABA concentration was determined on 1.0 ml. of the incubated blood. The PABA in the blood was determined as follows:

Ten ml. of distilled water were added to 1.0 ml. of blood and the proteins were precipitated by adding 4.0 ml. of 15% trichloroacetic acid, mixing the contents well. The mixture was then centrifuged and the clear supernatant liquid was filtered. Five ml. of the filtrate was pipetted accurately into a test tube and diazotized by adding 1.0 ml. of 0.1% sodium nitrite solution. After 3 minutes the excess of HNO_2 was destroyed by adding 1.0 ml. of ammonium sulfamate and after two minutes the diazotized solution was coupled with 1.0 ml. of 0.1% N-(1-naphthyl) ethylene diamine dihydrochloride solution. The blood blank on 1.0 ml. of blood with no added PABA was carried out simultaneously. The color developed is measured in a Beckman DU-spectro-photometer at a wave length of 545 millimicrons.

RESULTS

When 100 cases in each category were obtained the results were subjected to statistical analysis. Table I. It was found that the acetylating activity of the blood from the periodontal cases is significantly higher than that in normal blood.

DISCUSSION

It is difficult to interpret the meaning of the results obtained. If as reported by Becks, the blood pantothenic acid is low in periodontal cases then one would expect low acetylating activity, providing the pantothenic acid level was such as to form inadequate CoASH. The results indicate higher blood values in periodontal cases.

The acetylating activity of blood is dependent upon the acetylase activity,

TABLE I
Acetylation of PABA (%)

	Total No.	*Mean %*	*Stand. Dev.*	*t-ratio*	*Probability*
Control	100	27.3	±2.5	8.85	<0.001
Periodontal	100	30.8	±2.9		

CoASH and the presence of acetyl groups. Unfortunately we do not know the actual concentration of any of the variables. It is conceivable that with excess amounts of the enzyme, and sources of acetyl groups the CoASH could be suboptimum and still have high acetylating activity. According to Ostrom et al., blood from periodontal cases generally is higher in glucose, a prime source of acetyl groups. It is possible that this one factor alone may be responsible for the results obtained. It is further possible that as so frequently happens, the enzyme concentration may increase in order to compensate for some other deficiency.

On the basis of the results obtained it is quite obvious that our knowledge concerning the factors that regulate acetylating activity in blood is inadequate. Any sound interpretation of the results must await further investigation concerning this interesting reaction.

SUMMARY

The acetylating activity of the blood from 100 normal and 100 periodontal cases has been determined. It was found that the activity of periodontal blood is higher than that in normal blood. The results are statistically significant.

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A Correlation of Blood Constituents with Periodontal Disease
2. *e-Choline esterase*

by A. C. HUE, D. Y. BURRILL, L. S. FOSDICK, *Chicago, Illinois*

IN a previous paper it was reported that the acetylating activity of blood from periodontal individuals is higher than in blood from periodontally normal persons.[1] One of the common acetylation reactions is that involving choline. Acetyl choline is synthesized and excreted in certain nerve tissues during the transmission of the nerve impulse. The substance produced, acetyl choline, is pharmacologically active and toxic. This compound alters the permeability of the cell and also prevents another nerve impulse, so that before nerve conductivity is resumed the acetyl choline must be destroyed or hydrolyzed. Although acetyl choline is formed by choline acetylase in the presence of coenzyme A, the reaction is not reversible and hence the acetyl choline must be destroyed or hydrolyzed under the influence of other enzymes. A number of esterases will hydrolyze acetyl choline. It was thought that the specific enzyme, choline esterase, would attack the esters of choline only. A number of these esterases have been demonstrated in the blood, but the specific enzyme for the destruction of acetyl choline is thought to be that found in the erythrocytes and has been designated as e-choline esterase. It has been recently demonstrated that this enzyme is not as specific as was initially thought.

It is interesting to note that a number of compounds have been found which will specifically inhibit choline esterase. Such compounds as diisoprpyl fluorophosphate and physostigmine exert their toxic effects by virtue of the inhibition of e-choline esterase, hence allowing acetyl choline to accumulate. When this occurs no further nerve impulse can take place. The mechanism of action in the so-called nerve gases is that of inhibiting choline esterase.

In view of the theoretical considerations concerning this compound it was thought of interest to correlate the e-choline esterase content of normal blood with that of individuals suffering from periodontal disease.

PROCEDURE

Subjects were selected from among patients applying to the Clinic for service. Only those who presented clinical and radiographic symptoms of advanced periodontal disease, seemingly excessive for the apparent local causes, and those whose periodontal conditions were normal, were used in this study. Complete mouth exami-

This study was supported by a United States Public Health Grant, No. D-395 in the Chemistry Department, Northwestern University Dental School, Chicago, Illinois.

This report is based on a dissertation submitted to the faculty of the Graduate School of Northwestern University by A. C. Hue in partial fulfilment of the requirements of the degree of Doctor of Philosophy.

nations including radiographs were made, and if the patient was selected for the experiment a sample of blood was obtained and sent to the Department of Chemistry for analysis. After one hundred cases of each type were obtained, the clinical data was oriented with the chemical data.

For the estimation of e-choline esterase a modified method of McOsker and Daniel[2] was used. Two ml. of heparinized blood was centrifuged and the plasma decanted. The cells were then washed with 0.9% NaCl solution and again centrifuged. The layer of white cells that formed just below the supernatant was removed as completely as possible with a capillary tube with suction and the supernatant discarded. An equal volume of water was then added to the packed red cells in order to hemolyze them and this hemolyzed mixture was used for the estimation of e-choline esterase.

The reaction mixture consists of 0.39 ml. of 0.020 M solution of acetylthiocholine, 0.50 ml. of 1.5% tris-(hydroxymethyl) aminomethane buffer (pH 7.4), 0.10 ml. of 2.25 M sodium chloride solution, 0.10 ml. of 0.45 M magnesium chloride solution, and 0.21 ml. of distilled water. After equilibrating to 37°C, 0.10 ml. of hemolyzed solution of red cells is added to the above mixture, and the tube stoppered and incubated for exactly 10 minutes. At the end of the incubation period, 0.10 ml. of 50% trichloroacetic acid is added to the reaction mixture, the fluids mixed well and centrifuged. Six ml. of saturated sodium chloride solution are pipetted into a cuvette. One and two-tenths ml. of 2.0 M sodium carbonate (anhyd.) -0.90 M sodium cyanide mixture solution and 1.20 ml. of 0.091 M sodium nitroprusside solution are added to it. Immediately after addition of sodium nitroprusside, 0.60 ml. of the filtrate is pipetted into the cuvette. The blank solution is prepared by omitting the enzyme during the incubation. The hemolyzed solution is added after addition of trichloroacetic acid, and the blank solution is treated the same as above. The color developed is measured in a Beckman Du spectrophotometer in 30 seconds at a wavelength of 520 millimicrons.

RESULTS

It was found that the blood e-choline esterase in the periodontal cases is considerably higher than in normal blood. Table I. A statistical analysis of the results indicated that the difference between the values from normal blood and blood from periodontally diseased blood is significant.

DISCUSSION

The literature on choline esterase is in a state of confusion. Esterases that will destroy acetyl choline are in abundance in most tissues. The specific acetyl choline esterase, however, is much less widely distributed. Insofar as little was known regarding the specificity of the various esterases until recently, most of the literature is ambiguous regarding this factor. Nerve tissue is specially rich in the specific substance as is the e-choline esterase of red blood cells.

Blood choline esterase has been studied in relation to age, sex, and a number of diseases. It decreases with age.[3] After puberty the choline esterase is higher in men than in women but is particularly low in the blood of pregnant women.[4,5,6] These findings were not confirmed by Herschberg, et al.[7] High values have been found in Vitamin B deficiencies,[8] anxiety states,[9] high blood pressure,[10] diabetes mellitus,[11] allergy,[12] hyperthryoidism,[13] and in mental disorders.

The reason high or low values are obtained in the above states is not clear, nor is there an explanation for the fact that high values are found in the blood of periodontal cases. It may be a compensatory reaction to cope with the high acetylase values or it may be associated with the state of nutrition in regard to the Vitamin B complex. In any event, definite conclusions must be withheld until more is known

TABLE I
Statistical Data on e-Choline esterase (umols/ml/hr)

Total No.	*Mean*	*Std. Dev.*	*t-ratio*	*Probability*
Control 100	135.4	±5.6	9.30	<0.001
Periodontal 100	144.5	±7.6		

concerning these enzymes in the metabolic process.

SUMMARY

The e-choline esterase content of the blood of 100 normal cases and 100 periodontally diseased cases was determined. It was found that this enzyme is significantly higher in the blood from periodontal cases. The reason for this difference is obscure.

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THE WESTERN SOCIETY OF PERIODONTOLOGY

The Western Society of Periodontology Eighth Annual Meeting will be held in Las Vegas, Nevada, March 19 to 21, 1961. The guest speaker will be Dr. Robert F. Moyers, Professor of Dentistry (Orthodontics), University of Michigan School of Dentistry, Ann Arbor, Michigan. His presentation will include a discussion of the Development and Maintenance of Occlusion: (1) The original of Oro-Facial Reflexes; (2) The Establishment of Jaw and Occlusal Reflexes; (3) The Establishment of the Dental Occlusion and its Development; (4) The Rationale for Occlusal Equilibration; (5) The Correction of Deleterious Oro-Facial Habits.

For further information write Dr. Daniel Feder, 152 South Lasky Drive, Beverly Hills, California, or Dr. H. Leslie Levine, 9400 Brighton Way, Beverly Hills, California.

Correlation of Blood Constituents with Periodontal Disease
3. Acid and Alkaline Phosphatase

by A. C. Hue, D. Y. Burrill, L. S. Fosdick, *Chicago, Illinois*

THERE has been much work on phosphatases since their discovery in 1907 by Suzuki.[1] Little emphasis was placed on this group of enzymes until Harden and Young[2] found them in fermenting mixtures and Robinson[3] suggested that they were essential in bone formation. It is now known that there are numerous phosphatases, some rather specific. The non-specific ones, however, may be divided into two classes, alkaline phosphatase with an optimum reaction at 8.6-9.4 and acid phosphatase with an optimum activity at pH 5.0-6.0.

The acid phosphatase has been associated with the prostate gland and this enzyme is generally in higher concentration in the blood of cases with prostatic cancer.[4,5] The alkaline phosphatase is generally associated with diseases in which bone formation is retarded and in cases where there is marked bone resorption. The alkaline enzyme is formed chiefly in the osteoblasts. Hence any disease that will cause a proliferation of these cells should cause elevation of blood alkaline phosphatase. Elevated values are usual in osteomyelitis, hyperparathyroidism and Vitamin D deficiency.

Insofar as periodontal disease usually involves the absorption of alveolar bone there should be a local increase in alkaline phosphatase. Indeed Karshan et al. studying gingival blood did find increased alkaline phosphatase in individuals suffering from periodontal disease.[6] In an earlier reference he reported no significant difference.[7]

In view of the confusion that exists in this field it was decided to compare the blood acid and alkaline phosphatase activity of the normal and periodontal patients. In this investigation the acid and alkaline phosphatase activity was determined on both whole blood and blood serum.

This study was supported by a United States Public Health Grant, No. D-395 in the Chemistry Department, Northwestern University Dental School.

Work taken from a dissertation submitted to the faculty of the Graduate School of Northwestern University by A. C. Hue in partial fulfilment of the requirements of the degree of Doctor of philosophy.

PROCEDURE

Subjects were selected from among patients applying to the Clinic for service. Only those individuals who presented clinical and radiographic symptoms of advanced periodontal disease, seemingly excessive for the apparent local causes, and those whose periodontal conditions were normal, were used in this study. Complete mouth examinations, including radiographs were made, and if the patient was selected for the experiment a sample of blood was obtained and sent to the Department of Chemistry for analysis. After one hundred normals and 100 cases of periodontal disease were obtained the clinical data was oriented with the chemical data.

Acid phosphatase was determined by a modified Bodansky[8] and Woodard[9] techniques. Two ml. of buffered sodium β-glycerophosphate solution (pH5) are pipetted into a centrifuge tube. The solution is brought to a constant temperature (37°C), and 0.20 ml. of plasma (or whole blood) at the same temperature is added to it and the tube stoppered. The reaction mixture is incubated at 37°C for exactly 60 minutes. At the end of the incubation period, 1.8 ml. of 10% trichloroacetic acid is measured into the tube, the fluid mixed well and centrifuged. The following reagents are pipetted into cuvetts: 2.0 ml. of the filtrate; 2.5 ml. of molybdate-sulfuric acid reagent; 1.0 ml. of mono-methyl-para-aminophenol sulfate reagent; and 4.5 ml. of distilled water.

For blank solution, distilled water is used in place of plasma or whole blood, and treated same as above. The mixed solution is allowed to stand for 60 minutes, and the color developed is read at a wavelength of 680 millimicrons in a Beckman DU Spectrophotometer. The determination of phosphorous content in the sample before incubation is carried out simultaneously as follows:

Plasma (or whole blood), 0.4 ml. is pipetted into

Statistical Data on Acid Phosphatase (mg/ml/hr)

	Total No.	*Mean*	*Stand. Dev.*	*t-ratio*	*Probability*
Plasma					
Control	100	0.75	±0.23	0.31	0.4
Periodontal	100	0.76	±0.23		
Whole Blood	100	2.83	± .042	0.70	0.7
Periodontal	100	2.87	±0.39		

a centrifuge tube. One and six-tenths ml. of distilled water and 2.0 ml. of 10% trichloroacetic acid added to it, mixed well and centrifuged. Two ml. of the filtrate and two ml. of distilled water for blank are respectively treated the same as above, and the color developed is measured at 680 millimicrons.

A modified method of Gomori[9] was used for the estimation of whole blood and plasma alkaline phosphatase. Two ml. of buffered phenyl disodium phosphate (pH 9.5) are pipetted into a centrifuge tube. One tenth ml. of 0.002 M physostigmine is added to it. After equilibrating to 37°C, 0.10 ml. of plasma (or whole blood) is measured into the mixture and the tube stoppered. The reaction mixture is incubated for exactly 30 minutes at 37°C. At the end of the incubation period, 2.8 ml. of 8% trichloroacetic acid are added to it, and the fluid mixed well and centrifuged. The following reagents are pipetted into cuvetts: 2.0 ml. of the filtrate; 4.0 ml. of saturated alcoholic borax solution; and 1.0 ml. of 0.125% Red-BS solution. For blank solution, the 0.1 ml. of blood sample is omitted during the incubation. The test sample is added after addition of trichloroacetic acid and the blank is treated the same as above. The color developed is measured in a Beckman DU Spectrophotometer at a wavelength of 490 millimicrons after 15 minutes.

RESULTS

The results are shown in Tables I and II. It was found that there is no significant difference between the acid phosphatase of the normal cases and the periodontal cases in either whole blood or in plasma. The alkaline phosphatase however was higher in the blood from periodontal cases. This was true whether the analysis was done on whole blood or on plasma. In each case the T ratio was above 3 and the probability <0.001.

DISCUSSION

On the basis that all of the periodontal cases studied had suffered considerable bone loss and the normal cases had cost little or none, one might expect that the blood alkaline phosphatase would be elevated. This also confirms the observation of Karshan. The generalized rather than localized loss of alveolar bone would also indicate something systemic in nature. The elevated phosphatase however should be considered more as a result of bone loss than as a cause. In view of this it may be in order to search for some variable that would cause this loss. There is evidence that a number of

Statistical Data on Alkaline Phosphatase (umols/ml/hr)

	Total	*Mean*	*Stand. Dev.*	*t-ratio*	*Probability*
Plasma					
Control	124	4.42	±1.31	3.65	<0.001
Periodontal	124	5.12	±1.69		
Whole Blood					
Control	124	5.90	±1.80	3.50	<0.001
Periodontal	124	6.77	±2.10		

factors could cause such a phenomenon. Glickman has produced an osteoporosis by the use of cortisone but he did not measure the blood alkaline phosphatase activity of his experimental animals. Work also has been done with niacin and pantothenic acid deficiencies as well as protein deprivation. These experiments also produced bone loss similar to that in periodontal cases, but here again alkaline phosphatase was not determined. It would be well to investigate the relation of alkaline phosphatase to these variables.

SUMMARY

The blood acid and alkaline phosphatase activity was measured on 100 normal and 100 severe periodontal bone loss cases. No differences were observed in regard to whole blood and plasma acid phosphatase, but there was a marked difference in both whole blood and plasma alkaline phosphatase activity. The phosphatase was elevated in the blood of those with periodontal disease.

311 E. Chicago Ave., Chicago, Ill.

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THE CALIFORNIA ACADEMY OF PERIODONTOLOGY

The California Academy of Periodontology announces their Second Spring 'May' Conference Friday, Saturday and Sunday, May 19, 20 and 21 in Reno, Nevada. The program will include lectures, clinics in periodontics, entertainment, tours for the wives. For further information write Dr. B. O. A. Thomas, Program Chairman, 668 Homer Avenue, Palo Alto, California.

Effects of Air Drying on Rodent Oral Mucous Membrane: A Histologic Study of Simulated Mouth Breathing*

by JULES KLINGSBERG, A.B., M.S., D.D.S.,** LOUIS A. CANCELLARO, B.S., PH.D.,*** EARL O. BUTCHER, A.B., M.S., PH.D.,**** *New York, N. Y.*

CLINICAL studies on the effects of mouth breathing implicate air drying as a contributory factor in the etiology of gingival inflammation and edema.[1,2] Lite[3] has described several cases of mouth breathing in which the inflammation and edema were confined to the labial gingiva bordering the maxillary incisors. It has further been reported that the periphery of the affected area corresponds to the inferior border of the upper lip.[4] The implication is drawn that the lack of protection from the air produced the lesion. An examination of the literature has failed to reveal any controlled histologic studies on this subject. The aim of the present study is to examine the effect of air drying on the mucous membranes of rodents with regard to the production of inflammation and edema.

MATERIALS AND METHODS

Fifty 120 day-old Long-Evans rats and fifty 120 day-old Syrian hamsters were used in this study. The labial gingiva of the mandibular incisors was exposed to the air by surgically removing a portion of the lower lip[5] (Fig. 1). The cheek pouches of hamsters were also exteriorized using a modification of the method of Butcher and Johnson.[6] Everting the pouch by gentle traction with forceps produces a separation between the surrounding structures and the loose connective tissue of the pouch wall without detectable injury to vascular supply or innervation.[7,8] Pouches having necrotic lesions produced by vascular injury were discarded. This procedure results in a reversal of the histologic layers in that the epithelial lining becomes the outer surface (Figs. 2, 3).

Pouches were maintained in the extruded position for 17 days with the unexteriorized pouch of the same animal serving as a control. Verification of the validity of these controls was established by examining the pouches of unoperated litter mates. No differences were observed.

Tissues were fixed in Lillies AAF, embedded in paraffin, and stained with hematoxylin and eosin.

OBSERVATIONS

The gingiva of the lip-cut rats manifested a glistening appearance with no visible sign of inflammation or edema. It was hard on palpating (Figs. 4, 5). This appearance was always exhibited in rats but not in hamsters. Examination of gingival sections revealed an increase in thickness of epithelium and keratin in both rats and hamsters (Figs. 6, 7). No indication of inflammation or edema was evident.

Histologically the hamster cheek pouch consists of four distinct layers: 1) stratified squamous epithelium varying from two to five layers of cells with a small amount of keratin; 2) a lamina propria consisting of dense collagenous connective tissue fibers; 3) a layer of longitudinally arranged skeletal muscle which is derived from the buccinator, and which is absent from the blind end of the pouch; 4) a layer of loose areolar connective tissue into which the

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Histological material in this paper was taken in part from research performed in partial fulfillment of requirements for the degree of Doctor of Philosophy at New York University, Graduate School of Arts and Science.

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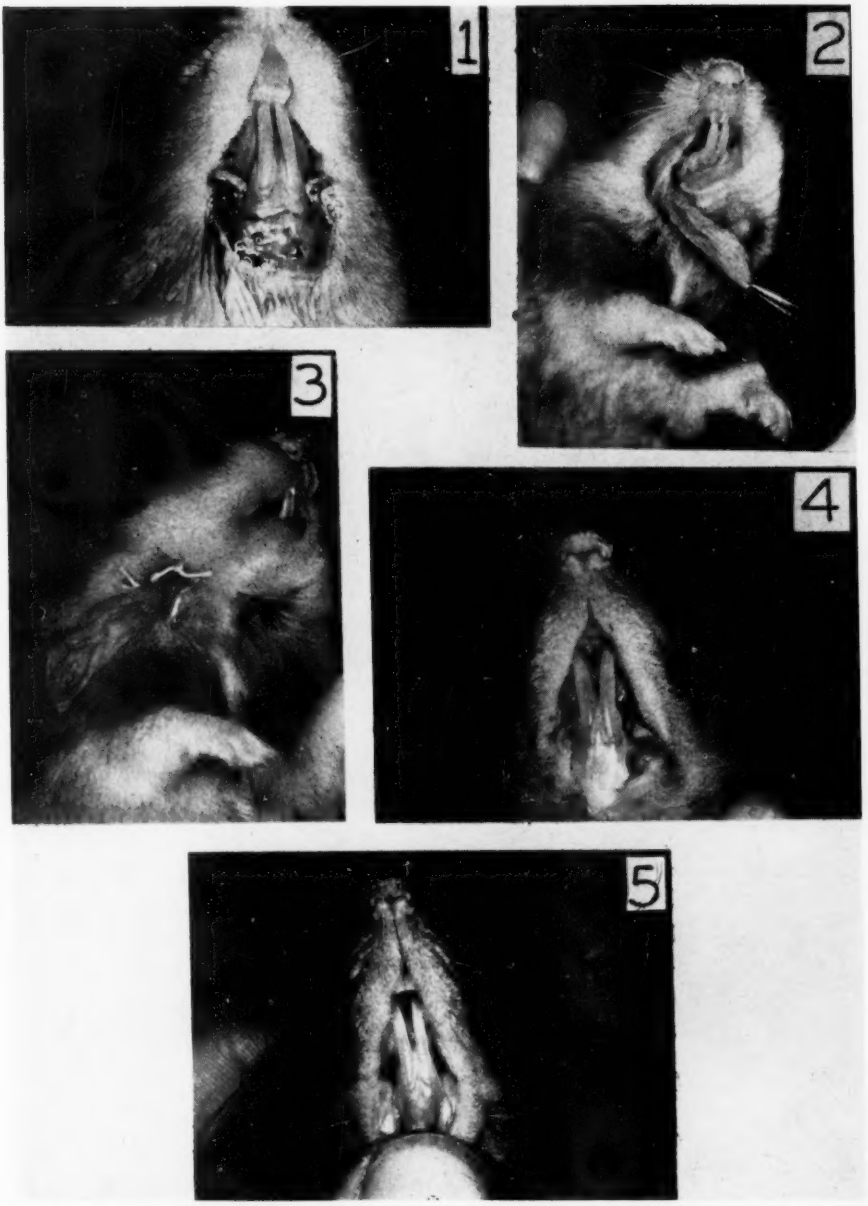

Fig. 1. Lip-cut rat immediately after surgical removal of lower lip. Fig. 2. Hamster undergoing exteriorization showing cheek pouch everted through oral cavity preparatory to insertion through skin of neck. Fig. 3. Hamster pouch exteriorization completed and pouch sutured into place. Fig. 4. Labial gingiva of lip-cut rat. Note glistening appearance of gingival surface. There is no indication of edema or inflammation. Fig. 5. Control for figure 4. Note absence of glistening white surface.

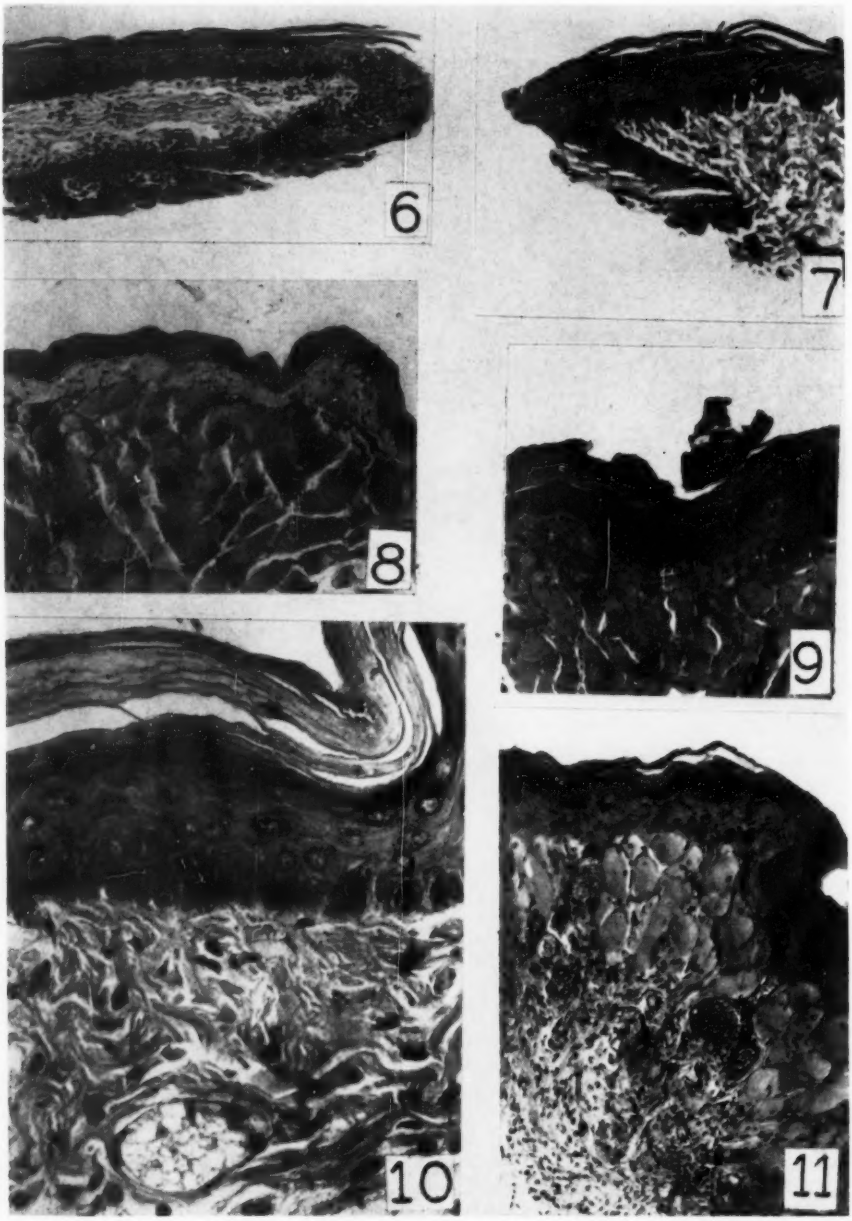

Fig. 6. Control section of labial gingiva of rat. H and E X 100. Fig. 7. Experimental (lip-cut) gingiva. The stratum corneum is increased in thickness but there is no visible increase in inflammation. H and E X 100. Fig. 8. Cross section of normal pouch. Note thickness of stratum corneum. H and E X 100. Fig. 9. Cross section of pouch exteriorized 17 days. There is an increase in keratin as compared with figure 16, but there is no evidence of inflammation in the tunica propria. H and E X 100. Fig. 10. Higher power of epithelium and tunica propria of exteriorized pouch showing normal morphology of epithelium, thickened keratin and absence of pathology in tunica propria. H and E X 300. Fig. 11. Cross section of exteriorized pouch showing inflammation deep in submucosa. H and E X 100.

retractor muscle of the pouch inserts. A complete histological study of the pouches is presented by Priddy and Brodie 1948.[9]

Sections of control pouches were found to have an epithelial layer of 30-50u of which 7-10u. was cornified (Fig. 8). A readily discernible increase in keratinization was observed in the experimental pouches. Measurements of the keratin revealed a 2 to 3 fold increase over the controls with no other alterations in the morphology of the epithelium (Figs. 9, 10). Some inflammation was observed deep in the submucosa of the exteriorized pouches in close proximity to capillaries (Fig. 11). This lymphocytic infiltration could be attributed to the slight trauma resulting from the surgical procedure. If drying of the mucous membrane was the cause of the inflammatory reaction, it would seem reasonable to expect inflammatory cells beneath the epithelium in the lamina propria and not deep in the submucosa as revealed by microscopic sections. No inflammation was observed in the lamina propria of any of the experimental pouches.

DISCUSSION

Exteriorization of the hamster cheek pouch has been found to induce an increase in keratinization of the pouch epithelium.

Keratinization may have been influenced by irritation due to the loss of the protection afforded by the oral fluids and by the direct contact with the atmosphere, or by alteration in fluid loss.

It has been previously shown[10] that tooth brush massage produces an increase in keratinization which is presumably due to the irritational effect. It has further been reported that the condition of the stratum corneum is related to the fluid loss, and that if water is lost from an epidermal surface at a more rapid rate than supplied, the stratum corneum dries out.[11] Therefore, it is possible that the combination of increased irritation and decreased external fluids have at least in part induced the increase in keratinization.

Human gingiva may differ from rodent gingiva in the response to air drying. The usefulness of rodent skin in determining the effects of irritants and other substances on human skin suggests that in certain respects rodent gingiva is comparable to human gingiva. The edema and inflammation found in mouth breathing in humans was not reproduced in the lip-cut and pouch exteriorized animals. This would seem to cast doubt on the belief that air drying produces edema and inflammation of the gingiva. It is possible that the contact of the upper lip with the gingiva which has been reported in mouth breathing impedes the removal of crevicular debris by saliva. This effect may be more potent than the air drying in producing the gingival pathology associated with mouth breathing. Thus the effectiveness of applications of vaseline in the therapy of mouth breathing gingivitis may be attributed to its mechanical stoppage of crevicular food impaction rather than the prevention of air drying.

SUMMARY AND CONCLUSIONS

1. A histologic study of the effects of air drying on the gingiva and oral mucous membrane of rats and hamsters has failed to demonstrate the production of inflammation or edema.

2. Air drying produces an increase in the keratinization of the oral mucous membrane and gingiva of rats and hamsters.

3. It is suggested that gingivitis associated with mouth breathing may be due to causes other than air drying.

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Book Review . . . .

Bone Homografts in the Surgical Treatment of Cysts of the Jaws and Periodontal Pockets, by Heyman Krømer. *185 pages, 64 illustrations. Oslo University Press, Oslo, Norway, 1960.*

This addition to the series of Norwegian Monographs on Medical Science is an elaborate 3-part report on the use of merthiolate-preserved human bone chips in jaw defects. Part I describes in considerable detail the results of 67 homografts and 3 autografts of bone in 60 radicular cysts, 6 fissural, residual or follicular cysts and 4 ridge defects. Periods of observation varied up to 6 years. Utilizing roentgenographic and occasionally histologic criteria, 51 cases were considered favorable, 14 partly favorable and 5 were judged to be failures. Part 2 concerns the treatment with bone homografts of 30 infrabony periodontal pockets with favorable responses noted in 23, partly favorable in 4 and failures in 3, roentgenographs and pocket measurement being used as the principle criteria. The grafted areas were observed from 1 to 3½ years. Part 3 involves similar treatment of 14 artificially produced periodontal pockets in 6 dogs with roentgenographic and histologic evaluation at various intervals from 14 to 100 days.

No evidence of sensitization was noted even in patients receiving 2 or more grafts and relatively few surgical or postoperative complications were noted. An adequate description of the preparation of the bone and of the surgical techniques used is presented as well as, commendably, a detailed discussion of the failures and partly favorable cases. There is excellent reproduction of preoperative and follow-up roentgenographs and photomicrographs as well as numerous well-executed line drawings. Clinical data of the case reports are presented in 2 separate charts in a cover pocket. The wealth of material is well presented and while not conveniently amenable to elaborate statistical or tabular treatment, it might be clarified by some relatively minor modifications in sequence or in elaboration of certain points. For example, the criteria used for the diagnosis of cysts were based on clinical and roentgenographic evidence and "as a rule, verified by histological observations," yet epithelial cells were not noted in 19 cases. Whether apical periodontal radiolucencies represent cysts, granulomas or cysts which have lost their epithelial linings because of acute exacerbations (as suggested by the author) would seem to be of fundamental importance in determining whether these lesions would have been expected to heal following adequate endodontic therapy alone or in conjunction with periapical curettage but without grafting. The inherent difficulties (recognized by the author) of accurate evaluation of bone homograft procedures of this type does not detract from the value of the work.

S. *Miles Standish*

Dentifrice Abrasion—Report of a Case*

by SUMTER S. ARNIM, D.D.S., PH.D.,** AND ESTES M. BLACKBURN, D.D.S.,***
Houston, Texas

IT HAS been 116 years since Goddard[1] wrote, "If too hard a brush is used, it irritates the gum, and sometimes, particularly if some gritty dentifrices are employed with it, denudes the necks of the teeth and causes their early loss." As the years have passed, much more has been written about the mysterious loss of tooth substances from the necks of teeth. Most authors used the term erosion to designate the condition characterized by notching of the necks, particularly on the facial surfaces, but W. D. Miller[2] suggested that this term serve only for those cases where the wasting was caused by unknown forces. As he and others[3,4] demonstrated the great variety of lesions that could be produced by the use of abrasive dentifrices, the term "dentifrice abrasion" came into general usage to denote the condition. It is used in this report to designate the progressive wearing away of hard tooth substance in the cervical area as the result of regular, vigorous, forceful use of an extra hard, natural bristle brush with generous amounts of toothpaste.

Lesions caused by these practices were produced during a ten year period by the patient described in this report. They are typical notches of dentifrice abrasion, save in one particular. They differ by being present on the lingual, mesial and distal surfaces of the teeth as well as on the facial. The depth of the notches, the rapidity of their formation and the involvement of lingual, mesial and distal, as well as facial surfaces, make this a rare case indeed. The cause of the condition, regular (2x daily), vigorous, prolonged brushing of the teeth with generous quantities of dentifrice, is well established by excellent records and an almost complete arrest of the wasting process since the patient was informed of the cause almost two years ago. In addition, basic fuchsin disclosing solution was used to determine the true nature of the denuded and notched surfaces. It showed no adherent microcosm[5] in those areas where the dentifrice was wearing the tooth substance away, but in those zones not reached by the patient's forceful brushings, microbial masses clung to the tooth surfaces in abundance. One might well say that this is a case, similar to many seen today, of over-brushing and under-cleaning.

CASE REPORT

The patient, a 49 year old man, was first seen in 1946. He has been an office worker throughout his adult life, has never had a serious illness, is not nervous and is not easily upset or disturbed. Roentgenograms were made at this time. No evidence of dentifrice abrasion or periodontal disturbances was observed. New films, Figs. I and II, were made from time to time as the patient returned for regular treatment including subgingival scaling and polishing every six months.

In 1951 the patient was instructed in the use of a hard, natural bristle, "professional" type brush and a modified Charter's[6] technic for cleaning his teeth. It was also at this time that the first signs of wasting at the necks were observed. The first evidence of loss of tooth substance seen in the roentgenograms is visible on the bicuspids in the films made in 1948 (Fig. I). The progressive loss of dental tissue, with increase in size and number of the lesions produced, is revealed in subsequent films (Fig. II).

The first photos of the teeth were made in 1956 (Fig. III). The lesions were well

*This investigation was supported in part by the Dental Research Division of The Procter & Gamble Company, Cincinnati, Ohio.

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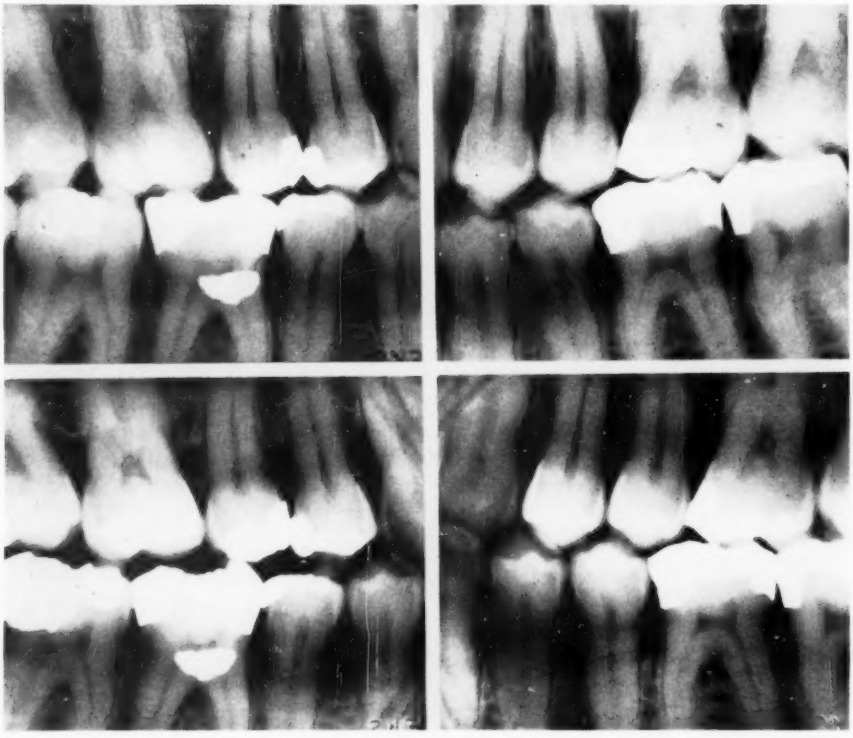

Fig. 1. Roentgenograms, top row September 1948, bottom row September 1954.

advanced at this time, and there was moderate recession of the gingiva with typical laceration of the soft tissues in the lower incisor area. The teeth were never sensitive and the gums were hard, stippled and heavily epithelialized. They hugged the necks of the teeth tightly.

As the loss of tooth substance continued to progress involving first the buccal surfaces then mesial, distal and lingual, every effort was made to determine the cause. Prolonged, extensive questioning revealed no history of the use of acidic foods or drugs, systemic disturbances, regurgitations, unusual dietary habits, unique cleansing technics, foreign substances held in the mouth or any conceivable explanation for the continuing, rapid progress of the lesions. Aqueous methyl red[7] was used to test the acidity of oral secretions and of the adherent microcosms. The tests revealed no acid present in saliva or on tooth surfaces. Microscopic examination of the adherent microbial masses showed a preponderance of coccal elements and an unusual scarcity of filamentous forms. Epithelial cells were common; few white blood cells were present and no red blood cells were observed.

Due to the unusual composition of the microcosms and the difficulty in visualizing them on the tooth surfaces, curiosity arose at this time (July, 1958) concerning their distribution. Photographs were made of the teeth to show how inconspicuous the microbial masses were; then basic fuchsin was used to disclose their presence. Surfaces not reached by the bristles of the brush were boldly outlined by the red stain (Fig. IV). The presence of thick, sticky masses of microbial material in areas difficult to brush,

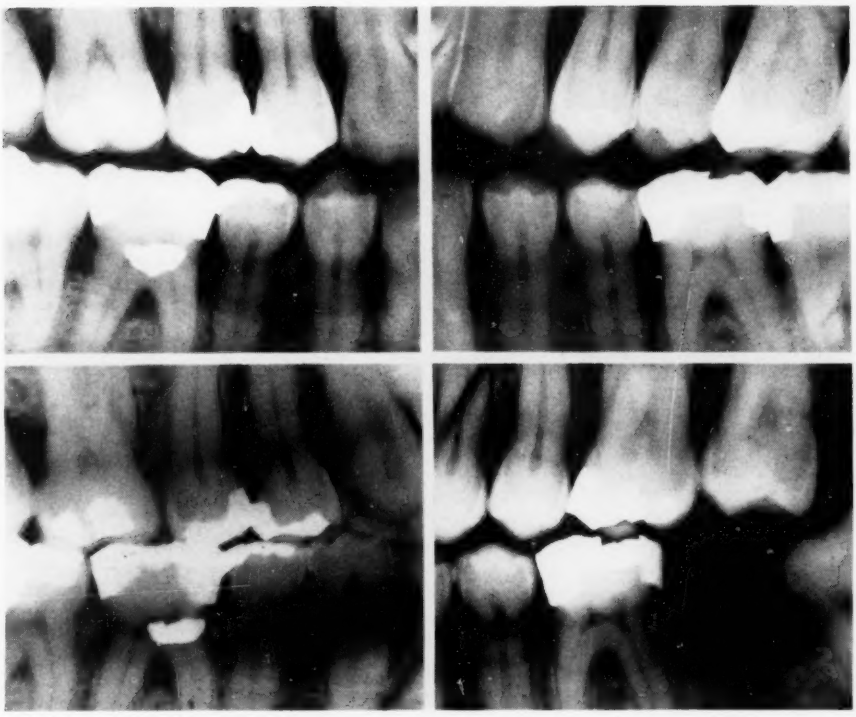

Fig. 2. Roentgenograms, top row November 1956, bottom row May 1958.

when compared to complete absence of microcosms in the areas cleaned thoroughly (including those lesions on the lingual, mesial, distal and facial surfaces) led to the question as to how the patient brushed his teeth.

When asked to demonstrate his technic, he took a new "professional" type, extra hard, natural bristle brush, grasped it with palm and thumb grip and forced it roughly into the interproximal spaces, rapidly pushing it to and fro (Fig. V). No water was used. When the patient was asked if the bristles hurt he said, "No Doc, this feels good," and increased the vigor and tempo of the brushing. He then demonstrated how

Fig. 3. Photos of the teeth made in 1956 showing notches at the necks and gingival recession.

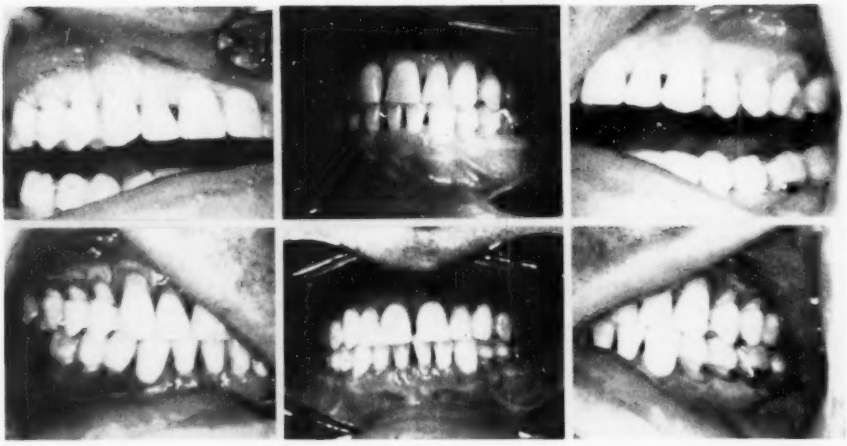

Fig. 4. Photos of the teeth made in 1958, upper row unstained, lowed row stained with fuchsin disclosing solution.

he reached the lingual surfaces of upper and lower teeth, leaving little doubt in the minds of the authors that he was the most thorough, enthusiastic and vigorous brusher they had encountered in their combined 60 years of dental teaching and practice. When the demonstration was ended, no evidence of gum lacerations or bleeding was seen. His gums were and are tough.

One question remained. It concerned the nature of the abrasive employed. The rapidity with which the lesions had progressed and their size could not be explained on the basis of hard, natural bristles alone.[4] The patient said he liked toothpaste and used it each time he brushed his teeth, before breakfast and at night before retiring. The trade names of brushes and dentifrice used are not mentioned in this article because the authors feel anyone could produce these lesions with any stiff brush and modern dentifrice if the brushing was as regular, forceful and prolonged as that employed by this gentleman.

Of course he was shocked to find that he

Fig. 5. Patient brushing with hard, natural bristle brush. Note strength and vigor displayed by palm and thumb grasp of toothbrush handle.

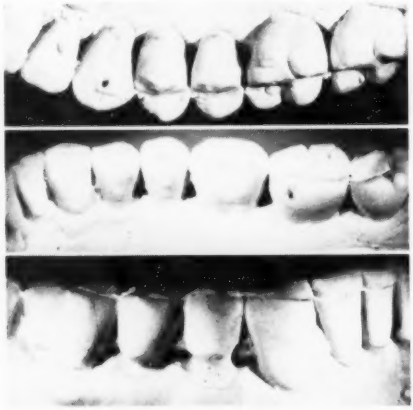

Fig. 6. Photos of models made from sectional impressions October 1958.

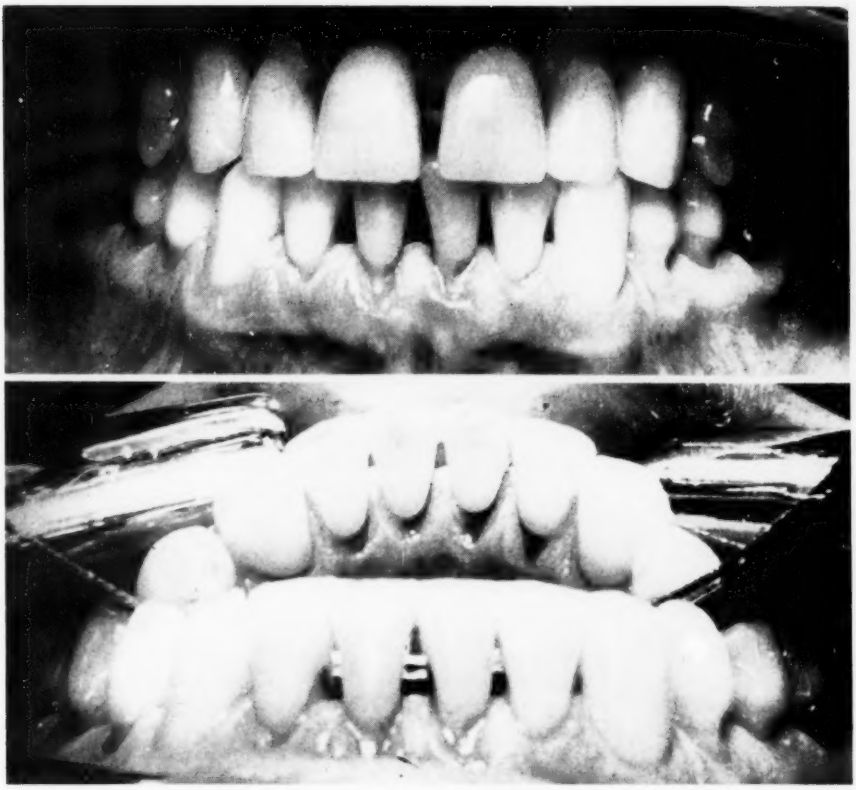

Fig. 7. Photos of teeth made January 1959, top—facial view, bottom—mirror view of lower incisors.

had been wearing away the teeth without cleaning them thoroughly at the same time. Examination of models (Fig. VI) made of the teeth and the use of fuchsin in the dental office convinced him this was true. He was given a small bottle of fuchsin for home use, soft bristle brushes, dental floss and instruction in the technics of personal oral hygiene.[8,9]

When last photographed, one year and five months later (December, 1959), the lower anterior teeth had less calculus than in the past. Also there was a thin, dark stain (pellicle)[10] that had not been present before. The lesions appeared unchanged otherwise (Fig. VII). They were certainly no larger and the teeth were not sensitive. The patient now brushes with a soft bristle brush, before breakfast and before retiring, uses a very small amount of the same paste, says he has to have some flavoring, and does a better job of cleaning as there is less adherent microcosm on his teeth as revealed by the disclosing solution. The presence of the clear, shiny, brown pellicle, lack of sensitivity and absence of microcosm all indicate that the teeth are cleaned effectively with a minimal loss of hard tooth substance. When the pellicle accumulates in such quantity that it is unsightly it is removed safely by the dentist.

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BERKSHIRE CONFERENCE — JUNE 18-22, 1961

The Twelfth Annual Berkshire Conference in Periodontology and Oral Pathology at Eastover, a resort hotel in the Berkshire Mountains in Lenox, Massachusetts; Sunday through Thursday, June 18-22, 1961. The theme of this year's conference will be "The Current Clinical Significance of Developments of the Past Twelve Years."

The conference curriculum is arranged so that the scientific sessions are held in the morning and evening and the afternoons are open for recreation and informal discussion. There is a complete program of activities for the Ladies. The conference is open to general practitioners and individuals in specialized practice. The following are the faculty and curriculum for the Twelfth Annual Berkshire Conference:

Joseph L. Bernier, D.D.S., M.S.—Major General, D.C., Assistant Surgeon General and Chief of the Dental Corps—*Developments in the Understanding of Malignancy as They Relate to the Diagnosis and Treatment of Oral Lesions.*

Irving Glickman, D.M.D.—Research Professor of Oral Pathology, Professor and Chairman of the Department of Periodontology, Tufts University School of Dental Medicine, Boston, Mass.—*The Status of Periodontics and the Problems it Presents.*

Sigurd Ramfjord, L.D.S., Ph.D.—Professor of Periodontology, The University of Michigan, School of Dentistry, Ann Arbor, Michigan—*A Step by Step Procedure for the Treatment of Temporomandibular Joint Disturbances by Occlusal Correction.*

John B. McDonald, D.D.S., M.S., Ph.D.—Director, Forsyth Dental Infirmary, Boston, Mass., Professor of Microbiology and Director of Post-doctoral studies, Harvard School of Dental Medicine, Boston, Mass.—*Bacteria and Enzymes: Their Significance in the Etiology and Treatment of Periodontal Disease.*

Frank Wentz, D.D.S., M.S.—Professor of Periodontology, Loyola University, Chicago, Illinois—*Muco-Gingival and Bone Surgery: Their Objectives, Advantages and Limitations in the Treatment of Periodontal Disease.*

Seymour Kreshover, D.D.S., Ph.D., M.D.—Assistant Director of the National Institute for Dental Research, National Institutes of Health, Bethesda, Maryland—*Systemic Factors: Their Significance in the Etiology and Treatment of Periodontal Disease.*

Finn Brudevold, L.D.S., D.D.S., M.S.—Chief of Dental Medicine, Forsyth Dental Infirmary, Boston, Mass., Professor of Dentistry, Harvard School of Dental Medicine, Boston, Mass.—*Research Advances in the Mechanism of Calculus Formation and Their Potential Clinical Application.*

David Weisberger, D.M.D., M.D.—Professor of Dental Medicine, Harvard School of Dental Medicine, Boston, Mass., Oral Surgeon and Chief of Dental Service, Massachusetts General Hospital, Boston, Mass.—*The Topical and Systemic Use of Drugs in Gingival and Other Oral Mucous Membrane Diseases.*

Everett Shapiro, D.M.D.—Associate Clinical Professor and Chairman of the Department of Orthodontics, Tufts University School of Dental Medicine, Boston, Mass.—*Orthodontic Procedures in the Management of Periodontal Problems.*

For further information and application write to: Tufts Berkshire Conference, Tufts University School of Dental Medicine, 136 Harrison Avenue, Boston 11, Mass.

Hypersensitive Teeth: Effect of Strontium Chloride in a Compatible Dentifrice

by MILTON R. ROSS, D.M.D.,* *Long Branch, N. J.*

DENTAL hypersensitivity probably affects most individuals at some time, and in some instances, pain may be so severe and so regular as to constitute a psychic problem for the patient who believes that his dentition has been seriously, and perhaps irreversibly, affected. Thermal, tactile, osmotic, and chemical stimuli are the most common causes of hypersensitivity and appear to operate by triggering the transmittance of neural impulses from external surfaces of the tooth to the dental pulp. Since nerve tissue in dentin has never been convincingly demonstrated, the referral of sensation probably occurs through the tubular lymph to the peripheral pulp nerves.[1] The fact that sensitivities are seen most often on buccal or labial surfaces, where there may be a higher incidence and degree of dental attrition,[2] demonstrates that sensitivity is usually associated with erosions, abrasions, caries, gingival recession, periodontal treatment, or other dental operative procedures.

An especially large percentage of patients undergoing periodontal therapy are sufferers of hypersensitivity prior to operative regimes and we have found that this condition may be aggravated during and after treatment. It has been well established that proper periodontal intervention will save many teeth that might otherwise be lost but the necessary techniques of occlusal balancing, gingival and alveoplastic recontouring and surgery, and other procedures frequently expose new dentinal and cemental areas to painful stimuli.

Some persons are sensitive to cold alone; others are sensitive to tactile impulses, heat, sugars, or to various combinations of these stimuli. There are probably qualitative variations in the histological characteristics of enamel and dentin from one individual to another that may, in part, explain the phenomenon of hypersensitivity and its differing manifestations. The commonly observed hypersensitivity to cold in children's teeth may arise because the tooth structure is less mature and less densely calcified, thus allowing more organic pathways for transmittance of stimuli.[3]

The treatment of dental hypersensitivity has been reviewed extensively,[1-5] and no practical purpose would be served by summarizing the various methods described in the literature. For use in conjunction with office practice, the ideal method would be one that could be applied in the manner of good home hygiene as a supplement to office procedures.

Recently, our attention was directed to a publication by a Polish investigator, who described successful results in treating dental hypersensitivity with applications of a 25 per cent aqueous solution of strontium chloride.[6] The author ascribed the action of the strontium chloride to its ability to combine with biocolloids of enamel and dentin through adsorption. Strontium is, if anything, less toxic than calcium, and has proved to be active in remineralization of bone.[7] Its safety and biochemical characteristics appeared to be sufficiently interesting to warrant an investigation of its value for the treatment of hypersensitive teeth. We have evaluated the agent in both solution form, in a small number of cases, and in a compatible toothpaste base containing 10 per cent strontium chloride,* which has been made available to us, in a larger group of patients.

MATERIAL AND METHODS

In 5 cases, treatment was conducted in the office with the 25 per cent aqueous

*Director, Dental Clinic, Monmouth Medical Center, Long Branch, N. J.

*Sensodyne, supplied by Block Drug Co., Jersey City, N. J.

TABLE I
Treatment with 10 Per Cent Strontium Chloride Toothpaste

Sensitivity to Various Impulses	*Degree of Relief*				
	Complete	*Good*	*Fair*	*None*	*Total*
Thermal only	34	6	4	4	48
Thermal and Sugars	9	0	0	1	10
Thermal and Tactile	7	0	3	0	10
Thermal, Tactile and Sugars	1	1	0	0	2
(Total Thermal*)	(51–72.9%)	(7–10.0%)	(7–10.0%)	(5–7.1%)	(70–100.0%)
Tactile only	1	0	1	0	2
Sugars only	2	1	0	0	3
Acid only	0	0	0	0	0
Tactile and Sugars	3	0	0	0	3
(Total Non-Thermal)	(6–75.0%)	(1–12.5%)	(1–12.5%)	(0–0.0%)	(8–100.0%)
Totals	57–73.1%	8–10.25%	8–10.25%	5–6.4%	78–100.0%

**Total Thermal*

Cold only 13, Heat only 1, Cold and heat 56, Total 70

solution of strontium chloride alone. This was applied with a cotton swab, by means of vertical pressure along the teeth toward the gingival tissue, after the tooth surfaces were dried with alcohol and warm air. All cases reported complete relief of symptoms within a few minutes of application. Our results appeared to confirm those previously observed.[6]

A total of 82 additional patients have been treated with the dentifrice, and results were available on 78. Of the remaining 4 patients, 3 moved away before any reports could be received from them, while the fourth claimed that the dentifrice "irritated her throat" and hence did not go on with treatment. This patient has had a long history of sensitivity reactions to various medications.

We have deliberately avoided simultaneous use of both solution and dentifrice in patients so that an objective appraisal of efficacy of each of the agents could be made without the question arising as to which was responsible for any observed action.

The test dentifrice used was a paste, having the formula:

Strontium chloride • 6H₂O	10.0 %
Deionized water	36.8 %
Polyols	24.0 %
Water soluble gums	1.8 %
Anionic Detergent	1.7 %
Nonionic Detergent	0.5 %
Diatomaceous silica	23.0 %
Flavor and saccharin	1.35%
Inert coloring agents	0.75%
Preservative	0.10%
	100.00%

According to the research department of the manufacturer, the formulation allows almost quantitative release of strontium ion on dilution with water by virtue of its avoidance of anions which could react with strontium ion to produce insoluble compounds.

Patients issued the dentfrice were carefully instructed in proper brushing techniques and given a multi-tufted soft nylon toothbrush. There was no need for special rinsing instructions because of the safety of the dentifrice.

When possible, the patients reported within a month of issuance of the denti-

frice, usually at periodic recalls, giving their estimates of the degree of relief, and when relief was first experienced. The patients' impressions were confirmed in the chair by observation of their involuntary responses to both artificially induced tactile and thermal stimuli. All patients were adults, except for one 14-year-old male. Of those in whom responses were obtainable, 55 were females and 23 were males.

RESULTS

The over-all results of treatment are summarized in Table I.

The tabulation indicates that thermal stimulus was the most frequent cause of sensitivity in our subjects. Seventy of the seventy-eight patients studied showed a painful response to application of cold and/or heat to tooth surfaces and of these, 22 were sensitive to other stimuli as well. Although the base of "non-thermal" sufferers is small (only 8 patients), the pattern of clinical results suggests about the same degree of effectiveness as in "thermal" patients. None of our patients were sensitive to acid foods or drinks although this type of stimulus has occasionally been indicated as a causative agent in hypersensitivity.

The results described were frequently achieved quite rapidly, usually within a week to a month from time of first use. In other instances, the final result came about by way of progressive improvement over a period of two to three months or longer. Only one patient showed a regression in response, going from "good" to "fair"; this patient had an objection to the taste of the test dentifrice. One patient exhibited complete relief from sensitivity in his upper teeth, and little benefit in his lower teeth; this was classified as a "fair" result. Complete relief was rapidly achieved in one case after other chair and home medications designed for the purpose had failed to produce any noticeable benefit.

Where good or excellent results were achieved, there appeared to be only minor differences, proportionately, among those who used the dentifrice once daily or more frequently. On the other hand, all five failures occurred among the patients who used the dentifrice only once a day. It is not possible, of course, to estimate whether improvement might have occurred in these patients if the frequency of use had been increased. In a number of cases patients, who stopped using the dentifrice after relief had been obtained, found that sensitivity returned. Resumption of therapy again resulted in elimination or marked reduction in symptoms. Most patients found the taste of the dentifrice agreeable, and considered that it had good cleansing properties and feel. Only two or three complained about the taste. Apart from the patient with an allergic history who claimed a throat irritation from use of the dentifrice, all patients showed excellent tolerance with no evidence of local reaction on hard or soft tissues of the mouth. The dentifrice had no apparent effects on silicate, acrylic, or metallic restorations.

The results indicate that strontium chloride solution and dentifrice present highly effective and well tolerated additions to dental therapeutics. The dentifrice is especially advantageous in that it is a nontoxic, nonirritating, and simple method for daily home use in the treatment of hypersensitive teeth.

DISCUSSION

It is of interest to examine some of the possible mechanisms involved in the action of strontium chloride on hypersensitive teeth. Pawlowska[6] suggests that the salt has some specific action on both the nervous system and the hard tissues, and emphasizes its capacity to "change the soft surface" of carious teeth with undeveloped enamel "into a hard and smooth one." Shorr and Carter[8] have shown that the addition of strontium to a given calcium intake results in greater remineralization of the skeleton than is possible with any amount of calcium alone.

Recalcification, however, would not ex-

plain the cessation of hypersensitivity that is sometimes observed within fifteen minutes or so after instituting therapy with the aqueous solution alone; recalcification cannot take place so rapidly. Similarly, if control of hypersensitivity were associated only with secondary calcification, it would be difficult to explain relapses upon cessation of treatment.

It appears logical, therefore, to suggest that the effect is primarily related to some influence upon the transmission of sensation. In the acellular, avascular tissue of the enamel and dentin, the connective tissue serves, in effect, as the chief circulation, cement, an ion exchange apparatus. It has been established that ions can penetrate the enamel and dentin from the saliva; i.e., that enamel acts as a semipermeable membrane, permitting the infiltration of ions from the oral surface.[6, 9-11] Sognnaes has stated " . . . the teeth are permeable to ions in both directions, and a certain turnover takes place in the enamel resulting mainly from the salivary secretion but, to a lesser degree, from the internal blood tubules, dento-enamel junction, and possibly, from the enamel spindles and tufts."[10]

Strontium has been shown to have greater power of filtrability through such semipermeable membranes than has calcium.[12] Further, it has been demonstrated that strontium chloride, in a concentration of .048 moles per liter can cause blockage of neural transmission of stimuli.[13] This concentration, equivalent to about 1.3 per cent, appears to be obtainable by the use of a 10 per cent concentration in a dentifrice as diluted by normal salivary flow and water used during toothbrushing. To these properties may be added the observation that strontium is strongly adsorbed on calcified tissues with a high organic content.[14] It seems reasonable to suppose, then, that strontium chloride acts by adsorption on or in the organic connective tissue of dentin and the dentinal tubular processes, with resultant blockage of impulses to nervous pathways.

In effect, one may postulate both a rapidly-acting mechanism that influences neural transmission, and a longer range mechanism that may involve both blocking of neural transmission and some stimulation of recalcification. A prime importance of strontium chloride application is that it avoids the use of caustics, protein denaturants, irritants, or toxic agents to effect relief of dental hypersensitivity. Since there are no known contraindications to treatment with strontium chloride, further laboratory and clinical investigation of its use seems justified.

SUMMARY

Treatment of dental hypersensitivity with a 10 per cent strontium chloride, ion-releasing dentifrice was undertaken in 78 patients. Good to complete relief was secured in 65 cases (83.3 per cent), while only 5 patients (6.4 per cent) failed to benefit.

Possible mechanisms of action are related to modification of transmission of neural impulses through tooth structure and to stimulation of recalcification.

Treatment was excellently tolerated, and commends itself as highly suitable for routine use. The dentifrice is well adapted for use in the same manner as ordinary home dentifrices. There are no known contraindications to its therapy.

255 Third Avenue

The author would like to express his sincerest appreciation for the valuable assistance by the staff of the dental clinic in the conduct of the study and by Mrs. Edythe Larsen in the compilation of data.

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Temple University School of Dentistry announces a special course Periodontia for the Periodontist—Advanced Surgical Techniques in Periodontal Therapy, to be presented March 25-29, 1961 from 9 a.m. to 5 p.m. daily.

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Tuition will be $300 and enrollment is limited.

For further information please write Dr. Louis Herman, Director, Postgraduate Studies, Temple University School of Dentistry, Broad Street above Allegheny Avenue, Philadelphia 40, Pennsylvania.

The Calculus Surface Index Method for Scoring Clinical Calculus Studies

by J. Ennever, O. P. Sturzenberger, and A. W. Radike, *Cincinnati, Ohio**

THIS study was conducted for the purpose of devising and evaluating a method for the clinical measurement of dental calculus formation. The ultimate objective was the validation of a scoring system for quantitating the accumulation of dental calculus in short-term testing programs.

There have been only a few clinical studies of potential anti-calculus agents. Kerr and Field,[1] Stewart,[2] Aleece,[3] Grossman,[4] Gunson,[5] and Jensen[6] all have attributed some effectiveness to the various treatments they tested. Except for Jensen, however, the authors based their conclusions solely on clinical impressions. Jensen used a severity scale for calculus. Unfortunately, the particulars involved were not closely described.

At this time there is a need for a dental calculus clinical scoring procedure. A suitable method should permit a relatively simple but meaningful evaluation of potential inhibiting agents.

METHOD

A series of preliminary observations led to the selection of the four mandibular incisors as the teeth to be graded. The choice was based upon the rate of calculus formation and the ease of observing the calculus on these teeth. In applying the scoring method, calculus was considered to be present if any amount, supragingival or subgingival, could be detected either visually or by touch. If the examiner were uncertain about the presence of calculus on a given surface, the surface was called calculus free. Each subject was examined in a dental chair under adequate artificial light. The teeth were dried with compressed air. A dental explorer #23 and a mouth mirror were the only instruments used.

Each of the mandibular incisors was considered on the basis of four surfaces, two proximals, one labial and one lingual. At examination, a number (zero to four) corresponding to the number of surfaces on which calculus had occurred was assigned each tooth. The total number of surfaces on which calculus was detected was considered to be the subject's calculus score and is referred to as the "Calculus Surface Index," (C.S.I.).

EXPERIMENTAL PROCEDURES

Fifty-six adults, selected because of histories of unusually high calculus formation, served as subjects. Each was given a dental prophylaxis and was assigned to Group I or to Group II, dependent upon a coin-flip. For two months, Group I received treatment X while Group II received treatment Y. The subjects were then graded for calculus by the C.S.I. method. Each subject received a second prophylaxis and was switched to the alternate treatment. After a second period of two months both groups were again graded.

The dental prophylaxis were done by one dental hygienist. All subjects were graded by each of two dentists, the same dentist always grading first. Neither dentist knew the scores given by his colleague, nor did he know the treatment schedule for any patient. A clerk recorded the findings and the examiners saw none of the data until the study was finished.

RESULTS

Table I contains the C.S.I. scores given each of the subjects by both examiners for the two test periods. Variation in agreement between graders for several individual subjects is apparent.

A comparison of the mean scores for each treatment shows a difference of 0.35 surfaces in favor of treatment X. At the

*Division of Dental Research, The Procter & Gamble Company, Cincinnati, Ohio.

TABLE I

Occurrence of Calculus Among 56 Selected Subjects Graded by 2 Examiners for 2 Successive 8-Week Periods

C.S.I. Scores for First Period					*C.S.I. Scores for Second Period*			
Treatment X		*Treatment Y*			*Treatment X*		*Treatment Y*	
Examiners					*Examiners*			
O.P.S.	*J.E.*	*O.P.S.*	*J.E.*	*Subjects*	*O.P.S.*	*J.E.*	*O.P.S.*	*J.E.*
		9	8	a	2	5		
8	5			b			10	8
1	4			c			3	4
1	2			d			4	2
		9	10	e	11	13		
12	14			f			16	16
		7	5	g	5	4		
		10	11	h	8	6		
1	2			i			2	5
		2	3	j	3	3		
		7	5	k	4	4		
		10	9	l	5	9		
5	6			m			6	6
		0	0	n	1	0		
5	2			o			3	4
9	10			p			7	9
		2	2	q	2	2		
		7	8	r	5	6		
5	5			s			5	7
10	8			t			8	7
		1	5	u	2	5		
		12	8	v	7	8		
13	4			w			15	13
7	7			x			7	8
1	2			y			3	1
10	8			z			8	7
		4	4	a′	4	3		
		9	8	b′	9	9		
		11	10	c′	10	10		
2	2			d′			2	3
		12	10	e′	7	6		
2	4			f′			1	4
2	3			g′			6	3
		9	10	h′	12	12		
		5	4	i′	4	3		
8	9			j′			7	7
		6	3	k′	6	6		
		7	5	l′	5	4		
		9	9	m′	10	8		
		4	11	n′	11	12		
1	5			o′			1	2
4	7			p′			2	2
8	8			q′			5	6
		7	8	r′	6	7		
4	4			s′			2	4
		10	8	t′	4	5		
2	2			u′			1	1
4	2			v′			3	2
		11	10	w′	13	9		
11	11			x′			10	8
8	10			y′			8	8
		12	9	z′	13	11		
		12	11	a″	11	10		
9	9			b″			8	7
		9	10	c″	8	8		
		11	10	d″	12	8		
27	27	29	29	n	29	29	27	27
153	155	224	214	Total	200	196	153	154
5.67	5.74	7.72	7.38	Avg.	6.90	6.76	5.67	5.70

0.05 level of probability this is not statistically significant.

The analysis shows an examiner-subject interaction. This is statistically significant at the 0.05 level of probability.

DISCUSSION

The data in Table I indicate a rather good agreement between examiners for the group of subjects taken as a whole. While this might be expected when examiners do their preliminary grading together it is worthwhile to know that the grading method lends itself to an acceptable uniformity of application. For individual subjects there was frequently a non-uniform disagreement between examiners. This most likely was brought about by the fact that the second examiner was grading surfaces that had been altered by the first examiner. Since this cannot be avoided, we believe it would be better to conduct clinical calculus tests using only one examiner whose ability to grade consistently has been demonstrated.

There was no difference in the scores between treatment X and treatment Y. A difference between treatments would have been statistically significant at the 0.05 level of probability if it had been as large as 0.54 surfaces. A study such as this would detect a difference of 1.08 surfaces approximately 95 per cent of the time.

TABLE II
Comparison of Treatments

Treatment	*Mean for Examiners* O.P.S.	J.E.	*Grand Mean*
X	6.30	6.30	6.30
Y	6.70	6.60	6.65

The error variance adjusted for the grading to be done by one examiner can be used to select the number of subjects needed to meet certain requirements for future studies of this type. Estimates of the number of subjects needed to insure that a difference would not be missed more than 5 per cent of the time are given in Table IV. These sample sizes also insure that an observed difference will not be falsely considered real more than 5 per cent of the time.

If we acknowledge that there was no difference between treatments in this study, the C.S.I. scores for the group may be considered to be quite constant over the two periods. This suggests that the

TABLE III
Analysis of Variance

Source of Variation	*df*	*SS*	*MS*	*F-Tests*	*F*	*.05*
Corr. Total	231	2,842.63				
Products	1	7.94	7.94		1.886	4.00
Periods	1	8.76	8.76		2.081	4.00
Groups	1	132.67	132.67		3.211	4.00
Subjects W. In Grs.	54	2,231.20	41.32		9.815	1.53
W. In Subjects	54	227.55	4.21		0.988	1.53
Judge	1	0.34	0.34		0.121	4.00
Judge X Product	1	0.11	0.11		0.072	4.00
Judge X Period	1	0.03	0.03		0.020	4.00
Judge X Subject	54	150.93	2.80		1.842	1.53
Residual	54	82.11	1.52			

TABLE IV

Estimate of Panel Size to Minimize α & β Errors in Split Panel Study

∂	N
0.5	438
1.0	110
1.5	49
2.0	28
2.5	18
3.0	13

∂ = difference
N = number of subjects

C.S.I. scores for the individuals are probably random. This interpretation should be considered with caution, however, until more information is available on the regularity of calculus occurrence in a calculus forming group of subjects.

Before we accepted the presence of calculus on a surface basis as our choice of criteria for detecting the degree of calculus formation, we examined a variation of the Calculus Surface Index. This was intended to provide a better estimate of the quantity of calculus present. The amount of calculus on each of the sixteen surfaces graded was recorded on a scale of zero to three. Use of the severity scale added nothing to the sensitivity of the C.S.I. method. This is to be expected in a short-term calculus study in which grading is done before extensive deposits of calculus have formed. For studies in which long-standing calculus accretions are to be graded, such a method for refining the quantitative aspect of calculus grading might be useful. This is indicated by the recent epidemiological study reported by Greene and Vermillion.[7]

SUMMARY

A simple method for grading dental calculus has been developed for use in short-term studies of the occurrence of dental calculus. Characteristics of the method, determined in applying it to a split panel comparative test, suggest its usefulness in evaluating treatments intended to affect dental calculus formation.

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ANNUAL SPRING SEMINAR

The Annual Spring Seminar sponsored by the American Academy of Periodontology will be held in Ann Arbor, April 24-26. Program details are to be found on page 87.

Psychogenic Factors in Recurrent Ulcerative Stomatitis and Idiopathic Orolingual Paresthesia

by CARLOS J. DALMAU, M.D., EDWARD V. ZEGARELLI, D.D.S., M.S., AUSTIN H. KUTSCHER, D.D.S., AND JAMES P. CATTELL, M.D., *New York, New York*

THIS study is a preliminary report attempting to determine what importance, if any, psychogenic factors play in the development of two clinical oral entities of essentially unknown etiology: recurrent ulcerative stomatitis and idiopathic orolingual paresthesia.

This research project was prompted by the observation of dental clinicians that these two entities were frequently precipitated or aggravated by stress or acute emotional crises. The help of the psychiatric department was sought in an attempt to establish a possible correlation of etiological significance.

Idiopathic orolingual paresthesia is characterized by subjective symptoms that may include pain, dryness, burning, itching, stinging, or boring sensations, or a sandy feeling in the mouth. Most of these complaints center about the tongue though other parts of the oral mucosa may be involved. Clinical examination is usually negative. If objective findings are noted, their minor character does not justify the degree of subjective complaints.

Ziskin and Moulton[1] described the following characteristics: (1) no observable lesions, (2) occurrence predominantly in post-menopausal women, (3) symptoms frequently referred to as persistent or unbearable, (4) complaints often associated with coexistent but unrelatable dental problems, and (5) prominent psychogenic factors. They concluded that there is a type of orolingual paresthesia (idiopathic glossodynia) occurring chiefly in post-menopausal women suffering from emotional conflicts, sexual maladjustment, and, frequently, cancerphobia, in which psychic factors appear to have an etiologic bearing. Reports by other investigators have not clarified etiology and pathogenesis.

Recurrent ulcerative (aphthous) stomatitis is another illness of undetermined etiology and non-specific therapeutic approach.[2-4] Although allergic, hormonal, infectious and traumatic factors have been investigated, the etiology is still unknown. This syndrome is characterized in its inception by vesicles that break down into ulcerations, usually from 1-12 mm. but occasionally 2-3 cm. in size. These may appear anywhere in the oral cavity, one or more at one time, recurring periodically, and lasting 10-14 days. Disappearance is soon followed by new crops with variable remission periods. The lesions are round or oval with irregular peripheries, covered by necrotic exudates or membranes, and are surrounded by an area of inflammation.

METHODS

All patients were originally seen in the Diagnosis Clinic of the School of Dental and Oral Surgery, Columbia University, for diagnostic study, close observation, and, in some cases, therapy, and were then referred to a psychiatrist for clinical appraisal involving one or more interviews. Thus, careful clinical evaluation invariably preceded the psychiatric interview. Only those cases are included in this report which received at least one psychiatric interview for evaluation. Two of the patients have had over three years of analytic psychotherapy and thus provide the possibility of a more comprehensive understanding of the problem. A total of 31 cases was evaluated: 12 patients (5 males and 7 females) with recurrent ulcerative stomatitis and 19 patients (4 males and 15 females) with idiopathic orolingual paresthesia.

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The findings of the research psychiatrist (CJD) were submitted to the senior research psychiatrist (JPC) for reevaluation and critique and also to the dental research team. Unfortunately, the negative and questionable cases cannot be entirely construed as such, since some patients resented a psychiatric inquiry, others were consciously or unconsciously uncooperative, and others presented character disorders and other defenses that made a comprehensive evaluation impossible. The advantage of our procedure, however, is that those cases which presented positive findings were so clear-cut that a simple diagnostic appraisal was possible. These observations were supplemented with another form of evaluation, the Cornell Medical Health Index.[5] These latter findings will be published later.

It should be emphasized that the oral symptoms of these two syndromes can be attended by anxiety, despair, worry, irritability, and, at times (particularly in recurrent ulcerative stomatitis wherein prodromal symptoms are noted), pathoneurotic complaints. These secondary reactions must be differentiated from emotional factors that may play a role in the initial development of these syndromes.

RESULTS

Viewed from the standpoint of the Oral Diagnosis Division, the paresthesias are less dramatic, clinically, than the striking signs and symptoms of recurrent ulcerative stomatitis. It became obvious from the beginning that psychogenic factors do play an important role in terms of the onset of lesions or at the time of aggravation of symptomatology of both disturbances. The psychiatrist also erred in a focal evaluation of the problem, which made the paresthesias a minor psychoneurotic symptom as compared to the lesions of the stomatitis, which diagnostically were of a more serious psychosomatic nature. Both concepts were proven wrong in the light of further investigation. The oral symptoms in both diseases were invariably accompanied by such other psychosomatic or psychogenic symptoms as to indicate a more generalized disturbance than the local oral disturbance implied. The following two cases will illustrate the above concept.

Case 1. A middle-aged man has worked for over thirty years for a company he dislikes and where he never made an adequate adjustment. He cannot resign at this time because he will lose all benefits accrued. The primary complaints when first seen were of cancerphobia and of diarrhea and abdominal pain. These difficulties were diagnosed as mucous colitis. During a period of crisis at his job, he developed an acute iritis, hypertension, pronounced overeating with marked weight gain, exacerbation of the colitis, and orolingual paresthesia.

The oral paresthesia taken in an isolated context would be a minor symptom from either a dental or psychiatric standpoint. When viewed in the totality of the patient, however, it represents but one component in a major constellation that spells a serious emotional disturbance. Any clinician who evaluated or treated any of these symptoms (within the realm of his own specialty) would probably make the same basic error.

Case 2. A 37-year-old female has been "nervous" all her life and has a history of anxiety reactions episodically. Since her marriage seven years ago, she has suffered from frigidity, vaginismus and dyspareunia; sexual fears and fear of pregnancy have also been prominent. Four years ago she had a stillbirth and following this developed a severe depressive reaction accompanied by bizarre fantasies and thoughts which disturbed her. She has been very afraid of dentists all her life and also presents phobia of darkness. Two years ago she developed recurrent ulcerative stomatitis. The significant point of the emergence of this symptom was that it coincided with the relief of her depression. In this case the oral symptoms appear as a direct substitution of the psychiatric symptomatology which is thus displaced and fixed in an organic psychosomatic illness.

The two representative cases presented show a condensation of all positive findings encountered in the other patients studied. The accompanying psychosomatic disturbances ranged from gastritis, gastric ulcer, colitis, and gall bladder disturbances, which frequently required surgery, to diabetes, hypertension, asthma, hay fever, migraine, et cetera. The list is impressive. A typical pattern is presented herewith: A patient with a well regulated hypertensive reaction is subjected to undue stress by the death of a close relative. These circumstances increase her responsibility for the care of other members of the family. At this time a reaction of oral paresthesia may come into existence. Theoretically, we would expect an increase in the blood pressure. However, many of our cases, rather than show an aggravation of pre-existing psychosomatic symptomatology, brought forth new symptoms to cope with the added stress.

DISCUSSION

The fluidity in symptom formation noted above brings a pessimistic reality into focus as far as a therapeutic approach in some patients is concerned. If we take Case 2 as an example and if we assume that we find a specific drug which will cure recurrent ulcerative stomatitis, what is the risk involved in possibly (reversing the process and) precipitating an acute psychotic depression? If the symptom is a substitution for an emotional disturbance, successful therapy at the Dental Clinic may mean just a new case at the Psychiatric Clinic. This is not a speculative possibility; we have in our data enough material to substantiate this hypothetical premise.

To allay any anxiety on the part of dentists, it should be noted that the same reversal process is frequently seen in psychiatric practice. One specific case treated for frigidity managed, after three years in therapy, to break through this block and achieve a vaginal orgasm. This was followed by a mild depressive reaction, headaches, an acute vaginitis, and hemorrhagic cystitis. Although these are exaggerated examples, they point nonetheless to a clear fact. As in physics, where energy and matter are found to be equivalent, in medicine the equation of emotional and organic may be the same with a mutually reversible direction.

It would be incorrect to infer that therapy should not be instituted for specific symptomatology, whether dental, medical, surgical, or psychiatric. However, awareness of the possibility that a displacement of symptomatology may occur as a result thereof will be helpful to the clinician and the patient. Two cases that were originally seen at the Ear, Nose, and Throat Clinic for ulcerative throat lesions were successfully treated there. They then came to the Dental Clinic with recurrent ulcerative stomatitis and orolingual paresthesias, respectively. Awareness of this psychosomatic continuum should be helpful in evaluating these cases.

Some of our negative cases were classified as such when, even in the presence of severe emotional disturbance, no direct correlation could be established with the presenting symptom. One case of recurrent ulcerative stomatitis underwent a comprehensive psychiatric evaluation one and a half years ago after an acute attack of Meniere's Syndrome. She suffers from migraine attacks two or three times a week, hypothyroidism, low back pain, and generalized gastrointestinal difficulties. However, the existence of the recurrent ulcerative stomatitis appears isolated from these other complaints. It is possible that a more comprehensive study with psychological testing techniques might show this case as positive rather than negative; however, we have preferred to rely on obviously positive cases.

This path of reasoning has led to the conclusion that psychogenic factors frequently play a significant role in the onset or course of these two conditions: at times as a causative or precipitating factor, at other times aggravating the symptomatology. We cannot completely rule out the influence of

emotional factors in those cases which appeared to be negative or questionable.

The following patterns were evident in those cases classified as positive:

(1) Direct substitution of psychiatric symptoms (anxiety, tension, depression) for oral complaints.

(2) Failure of a psychosomatic symptom (hypertension, asthma, colitis) to cope with added stress with resultant onset of either paresthesias or stomatitis.

(3) Success in therapy of psychosomatic complaint at another clinic, bringing forth a displacement of symptomatology at an oral level.

(4) A reversal of No. 3, where successful therapy at the Dental Clinic brings about the emergence of a psychosomatic complaint at another level. One case presented a gradual diminution of the recurrent ulcerative stomatitis as increased gastric distress was evident; at the time of psychiatric examination, the oral ulcerations had cleared up but the patient was being investigated for gastric ulcers.

We do not wish to imply that these two clinical entities are primary psychosomatic channels. There are many other dental complaints that may present similar problems. Rather, these two disturbances were selected for study to investigate the mode of operation of psychogenic factors in oral complaints in general. We hope to extend this project to other clinical entities of obscure etiology.

From the material presented it becomes obvious that a comprehensive medical history and a recent physical examination are essential to an adequate evaluation of the dental patient. Evaluation exclusively at the local level of the specialist (whether dental, psychiatric, or medical) is a gross error because of the fluidity of symptom displacement these patients present. The psychosomatic continuum observed in the evaluation of the cases presented indicates that any focal viewpoint is incomplete. At the time that the ear, nose, and throat clinic is congratulating itself on the successful treatment of a laryngitis, the dental clinic has acquired a new case.

One of the investigators (CJD) has treated two patients with oral paresthesias in analytic psychotherapy for over three years. This symptom should not be used per se as a basis to advocate psychiatric treatment. In spite of intensive therapy for a prolonged period of time, the symptom flares up whenever external or internal pressures build up. Both patients understand the symptom as a sign of stress and the need to resolve a conflict of environmental or internal nature. Both have run the gamut of symptomatology from anxiety, depression, and phobic reactions to orolingual paresthesias, gastritis, colitis, hypertension, iritis, obesity, et cetera. None of these symptoms are specific by themselves, though they do reflect a functional disturbance manifested at a psychic or somatic level.

The study of recurrent ulcerative stomatitis and idiopathic orolingual paresthesia has served as a basis for some broad generalizations. For example, in the few cases of lichen planus and geographic tongue with positive psychogenic findings whom we have studied we find essentially the same pattern as found in recurrent ulcerative stomatitis and idiopathic orolingual paresthesias. Why should the same conflict produce in one person anxiety, in another colitis, or recurrent ulcerative stomatitis, or lichen planus?

The fact that psychogenic factors can be causative in these syndromes should not warrant the inference that all such cases have this basis—any more so than that all cases of hypertension are psychosomatic in etiology. However, the role of emotional disturbances should be considered as a possible causative, contributing, or aggravating factor. Acute glossodynia may be seen after antibiotic therapy where a definite relationship to drug therapy can be established. The same reaction may occur at a later date, precipitated by emotional tension; thus, the same clinical syndrome may

occur with different etiological factors.

Earlier in this paper we have considered the therapeutic dilemma caused by the fluidity of symptomatology and the capacity for symptom displacement. In spite of the pessimistic note thus introduced, it is the responsibility of the clinician regardless of his field of endeavor to evaluate, diagnose, and treat the presenting complaint of a patient. Even though a psychosomatic element may be present, quite frequently these reactions are the result of transient stresses. To avoid therapy in order to obviate the possibility of symptom displacement is not wise; awareness of this possibility, however, will give a deeper understanding of psychosomatic processes.

Only a very small minority of the cases seen were good candidates for psychiatric therapy. Yet, there are ways in which the patients reported on can be helped without a lengthy and costly treatment process—a process which should be reserved for circumstances in which other symptomatology warrants psychiatric evaluation and treatment. It is not expected nor desirable that the dentist should "play psychiatrist." An interest in the patient as a person, however, can frequently reveal current problems that may be reflected in the patient's chief complaints. Sedation with meprobamate or barbiturates can frequently relieve such local symptoms. At times, for example, discussing the fact that as long as a serious marital problem exists there will be a reflection of this tension in this and other symptomatology may help the patient to either take an active role in the solution of his problem or to adopt a more resigned attitude towards the symptoms instead of jumping from doctor to doctor or clinic to clinic.

SUMMARY

A study was undertaken to investigate possible psychogenic factors in recurrent ulcerative stomatitis and idiopathic orolingual paresthesia. It became obvious early in the study that certain broad hypotheses could be safely formulated that encompassed not only dental but also psychiatric and medical psychosomatic problems as well.

The authors hope that the implications have been clear enough to stimulate other investigators to question or corroborate these findings or enlarge upon them.

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The authors acknowledge the appreciated assistance of Mrs. Florence Moore, Mrs. Helene W. Kutscher, and Mrs. Aldonna Skislak.

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ANNOUNCEMENT

The Department of Dentistry in Norfolk General Hospital is accepting applications for a mixed internship, with emphasis on oral surgery, and periodontia, beginning July 1, 1961. Applications should be addressed to Dr. Thomas G. Warrick, secretary, Department of Dentistry, Norfolk General Hospital, Raleigh Avenue, Norfolk, Virginia.

Healing Gingival Injury in Normal and Systemically Stressed Young Adult Male Rats

by S. S. STAHL, *New York, New York*

THE healing of an experimentally created interproximal periodontal injury has been reported.[1] It was noted that under experimental conditions, food impactions took place at the site of injury and thus acted as an additional irritant of the injured tissues. The present study was undertaken in order to observe the gingival tissue response to injury in an area relatively free from food impaction and to study the gingival healing processes in animals under generalized stress.

MATERIALS AND METHODS

100 Long-Evans strain male rats weighing an average of 267 gms. at the beginning of the experiment were divided into four groups.

Group A—36 animals received a gingival injury.

Group B—36 animals received a gingival injury in addition to an injection of 0.5 cc of turpentine into the hind leg daily for the first five days and three times weekly thereafter for a total of 30 days.

Group C—18 animals received 0.5 cc of turpentine in a similar manner and dosage as outlined for Group B.

Group D—10 animals were kept as untreated controls.

Animals were sacrificed in groups of two from Group A, two from Group B and one from Group C in accordance with the following time schedule: immediately after injury, 3 hrs, 6 hrs, 24 hrs, 48 hrs, 72 hrs, 96 hrs, 5 days, 7 days, 9 days, 11 days, 13 days, 15 days, 18 days, 21 days, 24 days, 27 days, and 30 days after injury. Untreated control animals were sacrificed at various times during the experimental period.

The gingival injury was performed under ether anaesthesia. It consisted of scraping of the maxillary gingiva of the alveolar ridge with a scalpel from the mesial surface of the first molar to the level of the second palatine ruga. This procedure removed the soft tissue to bone level, however, care was taken not to injure the bone itself. All animals were fed ad libitum during the experiment.

At the time of sacrifice, the jaw, salivary glands and adrenals were removed and prepared for histologic study. Serial sections were prepared from the jaw and salivary glands and were stained with Hematoxylin-Eosin, Wilder silver impregnation, Periodic acid Schiff stain with and without diastase digestion, and Periodic acid Schiff stain following 3 hour testicular hyaluranidase digestion.

GROSS OBSERVATIONS

Gingivally injured animals consistently gained weight during the experimental period which was only slightly below the weight gain of the nontreated control animals. Stressed and gingivally injured-stressed animals lost weight during the experimental period and almost never regained their starting weight (Fig. 1).

HISTOLOGIC OBSERVATIONS

For the sake of clarity, the observations will be reported by time intervals with the healing of gingivally injured rats described first.

Gingival Healing in Normal Rats

Thirty minutes after injury, the wound

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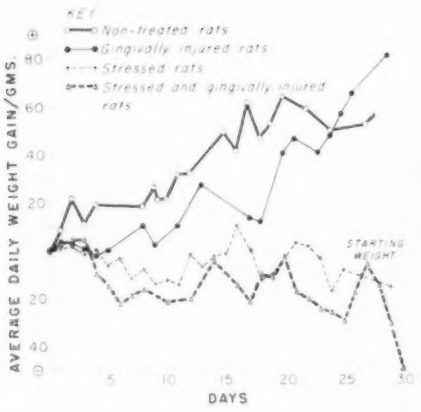

Fig. 1. Graph of daily weight increments in gingivally injured, stressed, stressed and gingivally injured and non-treated rats.

Fig. 2. Site of injury, 30 min. after injury. Hematoxylin-eosin stain. Magn. 140X. Note the homogeneous appearing collagen fibers below injury.

site showed a loss of epithelium and of some of the underlying connective tissue. The collagen fibers immediately below injury appeared slightly homogeneous and stained fuchsinophilic with the periodic-acid Schiff stain. The fuchsinophilia was not reduced by diastase digestion (Figs. 2 and 3).

A fibrinous exudate covered the wound surface three hours after injury. The collagen bundles immediately below the wound surface appeared homogeneous and a reduction of cementoblasts and to a lesser extent fibroblasts was noted in the area. The homogeneous appearing collagen bundles continued to stain fuchsinophilic with PAS stain (Figs. 4 and 5).

Six hours after injury showed the wound surface to be covered with necrotic debris and some cellular exudate. The loss of cementoblasts and fibroblasts in the area below injury was marked and the homogeneous appearing collagen fibers appeared more prominent. These changes persisted in the specimens taken 24 hours after injury. At this time an increase in inflammatory cells was present in the area. The altered collagen bundles remained attached to the cementum (Fig. 6). An increase in young, non-oriented fibroblasts was also seen in the more apical portions of the periodontal membrane.

Epithelial proliferation from the wound edges was seen 48 hours after injury. The epithelium proliferated upon a connective tissue base toward the tooth surface. Within the epithelium, an enlargement of the entire prickle cell layer as well as the individual cells was seen. No increase in mitosis was observed at this time (Figs. 7 and 8).

Marked cellular infiltration, composed primarily of round cells, was present in the connective tissue above the alveolar ridge 96 hours post-injury. The epithelium continued to creep forward and some pseudopeg formation was observed (Fig. 9).

Within the periodontal fibers below injury, young connective tissue cells were seen to invade the amorphous collagen which was still attached to the cementum. In some areas, orientation of young connective tissue cells was noted along the cemental wall. A similar orientation of

Fig. 3. Site of injury. Serial section of the specimen shown in Fig. 2 PAS stain. Magn. 140X. Note the fuchsinophilic (dark) fibers below injury.

Fig. 4. Site of injury. 3 hours after injury. Hematoxylin-eosin stain. Magn. 140X. Note the fibrinous exudate covering the wound and the reduction of cementoblasts and fibroblasts in the area below injury.

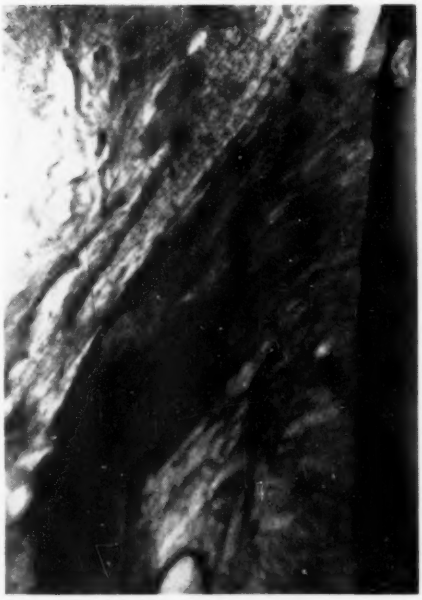

Fig. 5. Site of injury. Serial section of specimen shown in Fig. 4. PAS stain. Magn. 140X. Note the increased fuchsinophilia in the connective tissue below injury which corresponds in location to the homogeneous appearing collagen bundles seen in Fig. 4.

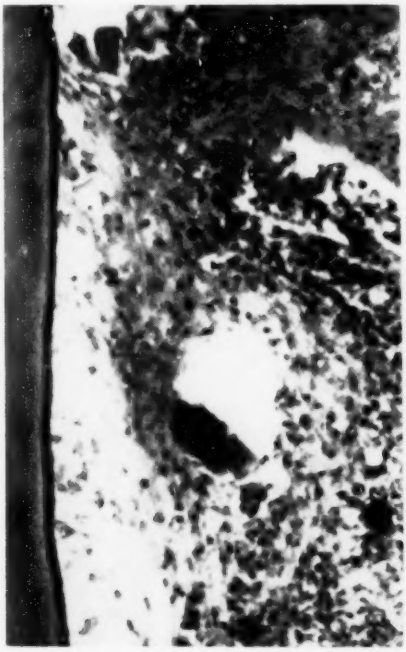

Fig. 6. Site of injury. 24 hours after injury. Hematoxylin-eosin stain. Magn. 140X. Note the inflammatory infiltration which does not extend into the homogeneous appearing but still attached collagen fibers at the cemental surface

Fig. 7. Site of injury. 48 hours after injury. Hematoxylin-eosin stain. Magn. 140X. Note the vasodilation below injury and the almost complete loss of cementoblasts and fibroblasts in this area.

young cells was also seen along the alveolar ridge surface (Figs. 10 and 11).

Five days after injury, the wound was covered with epithelium in most specimens. The epithelium appeared attached to the cemental surface coronally to the amorphous appearing collagen bundles. Many young connective tissue cells were present within the collagen below the wound surface and appeared oriented along the cementum and throughout the collagen bundles. The previously noted fuchsinophilia of the collagen below injury was markedly reduced at this time. The basement membrane, however, still stained prominently with PAS stain. Osteoblasts lined the alveolar surface and some osteoid formation was noted (Figs. 12 and 13).

With increasing time, further organization of the connective tissue at the wound site was observed. This was seen by an increase in young fibroblasts in the area which surrounded and involved the amorphous collagen and continuing osteogenesis at the alveolar crestal border.

Gingival recession with apical proliferation of the epithelial attachment was frequently observed in association with gingival plaques which began to form at the gingival crevice about 5 to 7 days post injury (Fig. 14).

Crestal osteogenesis became prominent 10 to 15 days after wounding and continued until 24 to 30 days post-injury (Figs. 15 and 16). An increase in well oriented cementoblasts lining the cemental wall also was noted during this interval.

The epithelium reduced in thickness 12 to 15 days after injury. At this time, an increase in mitosis in the basal layer of the covering epithelium was seen. Fuchsinophilia of the underlying connective tissue observed in the earlier specimens gradually became less notable while argyrophilic fibers appeared more frequently.

At the termination of the experiment (30 days) epithelization, organization of the underlying connective tissue and bone repair appeared to be complete.

Gingival Healing in Stressed Rats

The primary difference in the healing response of these animals in the first 24 hours post-injury, was a lesser fuchsinophilia seen in the collagen bundles below injury than was seen in the injured normal animals (Fig. 17).

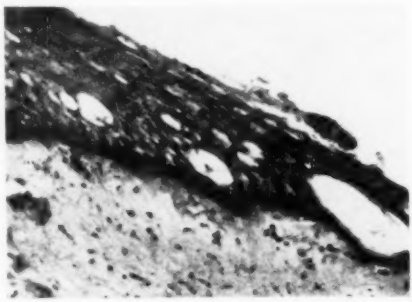

Fig. 8. Site of injury. 48 hours after injury. Hematoxylin-eosin stain. Magn. 140X. Note the prominent prickle cell layer at the proliferating epithelium.

After this time, a slower connective tissue organization was noted in the stressed animals. This became especially striking in the degree of crestal bone repair observed in the stressed animals as compared to the non-stressed group. At 24 days post-injury, the amount of bone regeneration in the stressed animals was significantly less than in the controls (Figs. 18, 19, 20). Epithelization of the wound, however, occurred within a similar time interval (4-6 days post-injury) in both groups of animals. This observation was especially interesting since the inflammatory infiltrate appeared more prominent in the stressed animals during the early days of the healing process.

Fig. 10. Site of injury. 72 hours after injury. Hematoxylin-eosin stain. Magn. 140X. Note young connective tissue elements orienting along the cemental surface.

DISCUSSION

The Standardization of the Wound

Studies in gingival healing have dealt primarily with tissue responses in humans or relatively large experimental animals.[2-7] The difficulty in obtaining patient cooperation for healing studies by time intervals as well as the inherent difficulties in handling larger animals make extensive studies in wound healing difficult. The present study suggests a procedure using a small laboratory animal which is easily performed and repeatable. Utilizing such standardized gingival injury as a baseline, healing under various metabolic variants may then be studied in comparable specimens. The use of a small experimental animal also enables the investigator to observe not only epithelial and connective tissue behavior, but also the bone and periodontal membrane responses of animals in easily obtainable sections.

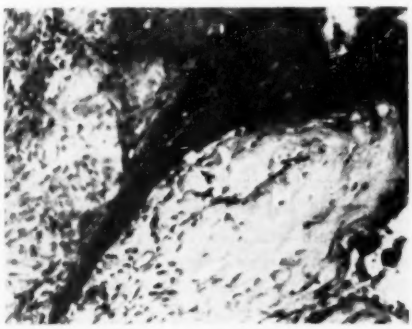

Fig. 9. Site of injury. 96 hours after injury. Hematoxylin-eosin stain. Magn. 140X. Note the pseudopeg formation.

The Epithelization of the Wound

The behavior of the tissues in the non-stressed injured animals showed facets in gingival healing which are similar to observations made in other wound sites. An initial matter of importance has been the relative value of the clot and the relation of the healing tissues to the clot. It has been noted in skin wound studies that epithelial proliferation occurs under the superficial clot and that the epithelial tissue proliferates on collagen. Weiss[8] points out that in mammalian skin wounds, the primary fibrin clot acts only as a dirt barricade, and that healing occurs when epithelial cells bridge across the wound under this superficial clot. Gillman[9] concludes from his

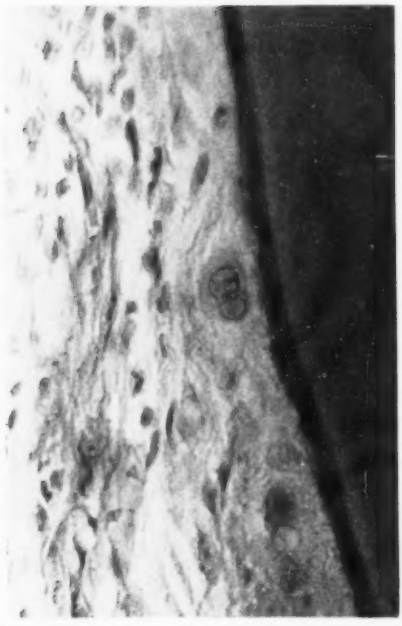

Fig. 11. Higher magnification of specimen shown in Fig. 10. Magn. 270X. Note the orientation of young connective tissue cells along the cemental border.

Fig. 12. Site of injury. 5 days after injury. Hematoxylin-eosin stain. Magn. 140X. Note the epithelium proliferating on homogeneous appearing collagen bundles and the appearance of young cementoblasts below injury.

studies in skin wounds that newly regenerated epithelium spreads across the wounds in direct contact with the denuded stratum reticularis of the dermis.

He too emphasizes that the new epithelium grows beneath the clot. In our specimens, epithelization was seen to progress directly on the denuded connective tissue surface even though some of the collagen near the cementum demonstrated degenerative changes.

A comparison might be drawn between this type of epithelization and the healing in extraction sites. In both instances, epithelial proliferation occurs a few days after injury. In socket healing, ingrowth of young unoriented fibroblasts into the coagulum has been described prior to the epithelization of the wound. However, here too, it was noted that epithelium proliferated under parts of the clot that failed to become organized.[10] Thus, epithelization progressed along the fibers of the old periodontal membrane and the new connective tissue. From a periodontal point of view, some differences may exist in the remodelling of the healing wound where a V-shaped crater exists as in the infrabony pocket compared with the healing of gingivectomy in a suprabony pocket. These differences await farther study.

A further comment should be made regarding the absence of increased miotic activity in the epithelium proliferating over the wound. The apparent widening of the prickle cell layer both as an entire layer as well as the enlargement of individual cells within the layer and the formation of pseudopegs have been observed in skin wounds[11] as has the widening of the basement membrane in the early stages of epithelization.[12] Lack of an increase in mitotic activity in the early stages of wound heal-

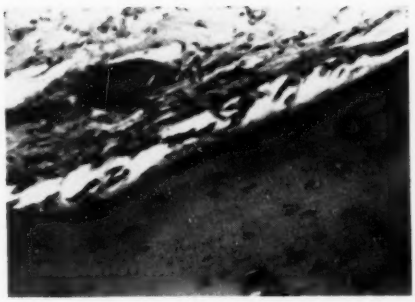

Fig. 13. Site of injury. 5 days after injury. Hematoxylin-eosin stain. Magn. 140X. Note the osteogenesis along the alveolar surface.

Fig. 14. Site of injury. 11 days after injury. Hematoxylin-eosin stain. Magn. 140X. Note the presence of a gingival plaque and the apical proliferation of the epithelial attachment.

ing has been described by Firket[13] who noted that in open skin wounds, migration of epidermal cells occurs first, with mitotic activity of the epithelium being a late phenomenon, apparently in response to migration.

The rate of epithelization of the wound in the stressed animals was equal to that observed in non-stressed animals. These observations are in agreement with general observations showing epithelization to take place when the animals are treated with corticoids either systemically or locally. This epithelization occurs even though the underlying connective tissue response is delayed.[14, 15, 16]

Healing of Connective Tissue

Of particular interest in our material was the rapid loss of cementoblasts followed by a loss of fibroblasts in the wound area. The loss of cementoblasts and fibroblasts occurred rapidly after initiation of the wound. The collagen bundles underwent degenerative changes comparable to fibrinoid degeneration seen in connective tissue injury. These bundles, however, remained attached to the cementum and served as a base upon which the new epithelium proliferated toward the cementum. They further showed an ingrowth of young fibroblasts, some of which eventually organized into cementoblasts as healing progressed. These altered collagen elements may thus be important in the subsequent level of the epithelial attachment. It should be noted, that later stages of healing showed an apical epithelial proliferation along the cementum in some specimens. Why this proliferation took place in some instances and not in others may be related to subtle changes in the mode of attachment of these bundles, or possibly to the speed with which new connective tissue elements invade the degenerating collagen fibers.

The present study further demonstrates the interrelation between various phases of wound healing. An initial increase in mucopolysaccharides at the wound site was observed in our specimens which was partially hyaluranidase labile. The increase was most striking in the early hours following injury and then gradually diminished. These observations agree with previous findings in both skin[18] and gingival wounds.[6, 17]

Following the initial response, inflammatory cellular infiltration reached a peak at about 24-48 hours after injury after

Fig. 15. Site of injury. 11 days after injury. Hematoxylin-eosin stain. Magn. 140X. Note the increasingly evident bone deposition along the alveolar surface.

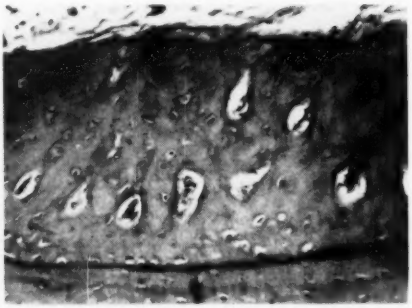

Fig. 16. Site of injury. 24 days after injury. Hematoxylin-eosin stain. Magn. 140X. Note the marked crestal apposition along the alveolar surface.

which time it slowly decreased. Epithelization of the wound and repair of the underlying connective tissue began at about that time. Epithelization of the wound was usually complete at about 5 days past injury while organization of the connective tissue elements took a much longer time. This also has been observed in the study of extraction wounds.[19]

It should be noted that the proliferation of mucopolysaccharides appeared less marked in the stressed animals than in the non-stressed group. Proliferation of young connective tissue cells and organization of these elements also appeared to be delayed in these animals. This slower response appears similar to that reported in wound healing in cortisone treated animals where a reduction in ground substance and granulation tissue has been reported.[20, 21]

The margin of the alveolar ridge showed initial infiltration of inflammatory cells into the vascular channels of the bone which was associated with alveolar resorption, thus demonstrating the response of the underlying bone to gingival inflammation.[22]

Healing Response of Bone

New bone formation was noted to begin about 5-7 days after injury while an osteoblastic differentiation was noted somewhat earlier. This time interval was similar to that observed in extraction sites where new bone formation was described 5-7 days after extraction,[23, 24] and in fractures where differentiation of simple connective tissue cells into chondroblasts and osteoblasts has been reported to occur 3 to 4 days after injury.[25] New bone formation continued to a marked degree in the older specimens.

In contrast to these observations, crestal bone apposition was almost never seen in a previous study[26] where an interproximal injury was created. It was postulated at that time, that the marked crestal resorption and gingival recession which took place with an interproximal injury, reflected the continuous irritation associated with food impactions at the site of injury. In the present specimens, gingival recession was observed in some instances and at times associated with plaque formation. These observations focus on the importance of local environmental conditions on the healing behavior of the gingival tissues. Of further interest was the time interval after which recession and plaque formation was first noted. Further studies are necessary to elucidate the reason for this time lapse.

The marked difference in the degree of new crestal bone formation between the injured and injured-stressed animals was most striking. While marked crestal osteogenesis was noted in the injured animals, it was never observed to the same degree in

Fig. 17. Site of injury. Stressed animal. 30 min. after injury. PAS stain. Magn. 140X. Note the lessened fuchsinophilia of the connective tissue below injury as compared to fig. 3.

Fig. 18. Site of injury. Stressed animal. 5 days after injury. Hematoxylin-eosin stain. Magn. 140X. Note the lesser repair of the underlying connective tissue seen in this specimen as compared to the repair seen in Fig. 12.

the stressed-injured animals. Similar interferences with bone formation have been reported in animals on dietary deprivations[27] and may denote a metabolic interference with osteogenesis.

The crestal bone deposition which took place in our specimens after gingival injury focuses attention on the possibility of repair following gingivectomy and gingivoplasty procedures. The difference in amount of osseous regeneration following injury noted between the non-stressed and stressed animals suggests possible pathways in which systemic stressors may influence the ability of osseous repair in patients.

A final comment should be made regard-

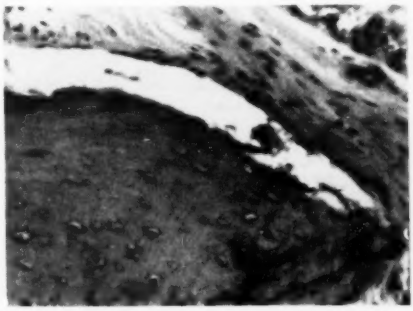

Fig. 19. Site of injury. Stressed animal. 15 days after injury. Hematoxylin-eosin stain. Magn. 140X. Note the lack of osteogenesis along the alveolar surface. The space between the bone surface and connective tissue is an artifact.

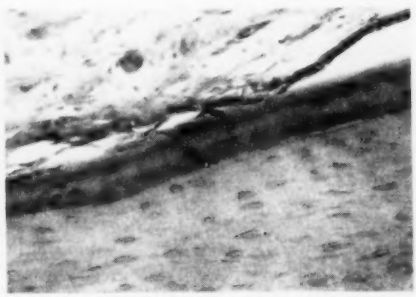

Fig. 20. Site of injury. Stressed animal. 24 days after injury. Magn. 140X. Note the lesser crestal apposition present in this specimen as compared to the specimen shown in Fig. 16.

ing the possible significance of the apparently normal epithelization and delayed connective tissue repair seen in the gingivally injured-stressed animals. Piram and Levenson[29] have observed that healed wounds broke down when animals were made scorbutic 2 to 6 weeks after injury. These observations as well as the observations recorded above suggest the possibility of a latent influence of metabolic imbalances on gingival injury and repair patterns which might be significant in the study of oral and systemic interrelations.

SUMMARY AND CONCLUSIONS

A repeatable gingival injury was inflicted upon normal and stressed young male rats. Animals were sacrificed in small groups following varying time intervals and the behavior of the tissues in the wound was studied.

It was noted that stressed animals lost weight while weight gain was routinely observed in the non-stressed animals.

Histologically, initiation of the wound was followed by alterations of the periodontal membrane in the wound area. The alterations consisted of a loss of cementoblasts and fibroblasts below injury and fibrinoid degeneration of the collagen fibers. These changes were seen in association with an increase of fuchsinophilic material, probably mucopolysaccharide in nature, in the wound area which became prominent during the early hours following injury.

Inflammatory cellular infiltration was initially observed after 6 hours and became prominent 24 hours after injury. Proliferation of epithelium from the wound edges was noted after 48 hours and was associated with both a gradual reduction in PAS positive material and inflammatory infiltrate in the wound area.

Epithelium was seen to proliferate over connective tissue elements including the altered collagen fibers which remained attached to the cementum. An enlargement of the prickle cell layer behind the proliferating epithelium was noted, however, an increase in mitosis was not observed in the proliferating epithelium. The wound surface was epithelized after about 5 days.

Following epithelization, organization of the underlying connective tissue took place at the site of gingival injury. This organization consisted of an increase in young connective tissue elements which later differentiated into oriented fibroblasts, cementoblasts and osteoblasts. A reduction in fuchsinophilia and argyrophilia in the connective tissue below injury was observed as healing progressed.

New bone formation at the alveolar ridge surface was first seen about 5-7 days post injury and became very prominent in the older specimens.

Gingivally injured - stressed animals showed a delay in the organization of the connective tissue in wound areas and a striking reduction in osseous regeneration of the alveolar ridge as compared with that observed in the wounds of non-stressed rats.

The author gratefully acknowledges the technical assistance of Miss Helen Rosenman A.B., in the preparation of this study.

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The University of California School of Dentistry announces a course in Dynamics of Periodontics Friday, February 24, and Saturday, February 25, 9 a.m. to 5 p.m. The course, to be held in Classroom F, fifth floor of the University of California Hospital Building at Third and Parnassus Avenue, San Francisco, will include lectures by Dr. Perry A. Ratcliff and Dr. R. Earl Robinson.

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Tuition for this course is $40.00. For further information please write Dr. Ben W. Pavone, Coordinator, Postgraduate Education, School of Dentistry, University of California, San Francisco Medical Center, San Francisco 22, California.

Alveolar Bone Changes in Sickle Cell Anemia

by GEORGE MITTELMAN, B.S., D.D.S.[1]; BURTON F. BAKKE, D.D.S.[2]; IRWIN WALTER SCOPP, B.S., D.D.S.[3], *New York, N. Y.*

ALTHOUGH a great deal has been written about sickle cell anemia from a medical standpoint, the dental aspects of the disease have not received adequate emphasis in the dental journals; nor has a complete description of the roentgenographic findings in the maxilla and mandible been made. Four patients hospitalized for this disease at this installation all showed characteristic roentgenographic changes in the maxilla and/or mandible.

Sarnat and Robinson[1] reported on 22 cases in whom there were detectable changes in the jaws in 79.2% of the cases as compared to 13.6% of changes found in the long bones and only 4.5% in the skull. A plausible explanation for the predominance of jaw changes in contrast to changes in other bony structures will be presented later. However, if the above percentages hold true for a majority of all patients with sickle cell anemia, then the dental profession is in a unique position to aid in the diagnosis and detection of the disease in undiagnosed, or suspected cases.

DEFINITION

Sickle cell anemia is "A chronic hereditary and familial hemolytic anemia, confined with few exceptions to Negroes or those with an admixture of Negro blood, thought to be due to an intrinsic defect in the erythrocyte and characterized by the appearance of a considerable number of sickle shaped red blood cells in the circulating blood, the symptoms of an anemia, recurrent leg ulcers, cardiovascular manifestations, and acute episodes of abdominal pain, jaundice, nausea and vomiting."[2]

HISTORY

In about 1840, reference was made to the presence of abnormally shaped red cells in certain species of wild deer. More recently, reference has been made to findings similar to those seen in human sickle cell anemia among deer found in Michigan.[11]

In 1889, Hayem in his book "Blood and its Anatomic Variations," mention is made of crescent shaped red cells. In 1905, Sergent and Sergent found "half moon corpuscles" in about 5% of 234 natives of Algeria. However, since all these patients had malaria, they attributed this finding to malaria.

Although several other observers reported findings of abnormal circulating red cells, it was James Herrick[4] in 1910 who presented the classical clinical picture of this disease. Mason[5] was the first to give the disease the name "Sickle Cell Anemia." Neel[6] made a valuable contribution in showing the hereditary nature of the disease and Pauling[7] and his associates in their studies of hemoglobin by the use of electrophoretic methods, demonstrated that there was an abnormal hemoglobin present in the red blood cells of patients with sickle cell disease. Some of these abnormalities will be discussed later as well as a number of other abnormal hemoglobins that have since been found.

CLASSIFICATION OF HEREDITARY ANEMIAS

In order to obtain a clearer picture of the place into which sickle cell anemia fits in relation to the larger picture of Hereditary Anemias in general—those anemias in which there is an intracorpuscular defect—Watson's classification slightly modified to bring it in line with more recent findings has been adopted.

I Congenital Hemolytic Anemia
II Thalassemia Major and Minor
III Sickle Cell Anemia
IV Combinations—to be discussed later
V Hereditary Non-Spherocytic Hemolytic Anemia
VI Ovalocytosis

It will be seen, later, that this classification is one of convenience alone, since most of these varieties of hemolytic anemia can be explained to a large extent by mathematically calculating two gene combinations as will be done later.

THE HEREDITARY NATURE OF THE DISEASE

In its search for knowledge science very often uncovers many other apparently unrelated facts that shed light on related problems. Since the discovery by Pauling

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of the abnormal hemoglobin S—or sickle cell hemoglobin, and by the use of electrophoretic, biochemical, solubility, immunological, physicochemical, and other methods, no less than six other abnormal hemoglobins have been found, and it is likely that more will be added to the list. Studies show that the qualitative production of hemoglobin is under genetic control. At the present time, the following hemoglobins and hence the genes to elaborate them are known to exist: HbA (adult) HbC, HbD, HbE, HbF (fetal), HbG, HbH, HbS (sickle cell) and Hb Th (Thalassemia). If the two gene combinations are studied, omitting HbF as was done by Zuelzer[15], then 36 possibilities can be worked out, beginning with a normal individual with HbAA genes and ending with Hb Th Th, an individual with Thalassemia Major. Using this table, many of the puzzling hemolytic anemias of the past can be explained, and the others predicted. The problem of abnormal hemoglobin production is far more complex than the simple table enumerated above, as it does not take into account the possible interaction of genes, nor of all possible abnormal genes yet to be found, etc.

Returning to the problem of the hereditary nature of sickle cell anemia, one must differentiate between those persons exhibiting the sickle cell trait (sicklemia) and those manifesting the disease itself. The trait carrier has a genetic makeup which can be represented as (S+A). The presence of these two types of hemoglobin can be seen on an electrophoretic strip where, by a comparison of the patterns made by Hb A and Hb S, the trait hemoglobin will show the presence of both globin moieties.

Genetically, if two trait carriers produce offspring, then according to the Mendelian laws of heredity, 50% will show the trait —the heterozygous condition, 25% will manifest the disease since they have the SS genes and are therefore homozygous, and 25% will have neither the trait nor the disease. Neel[6] observed only two exceptions to this rule. Patients with the trait do not present evidence of the disease. There is no anemia, no evidence of increased hemolysis, no evidence of increased blood regeneration, the white cell count is normal and the red cells are sickled in vitro with some difficulty. There is no evidence that people with the trait develop sickle cell anemia, nor that those with the disease show a remission leaving only the trait.[9]

INCIDENCE

About 8% of American Negroes have red cells that can be sickled in vitro—i.e., have the "trait" with no symptoms. About 0.2% have the symptoms of the anemia. Here the red cells sickle in vivo as well as in vitro.[8] Both males and females are equally susceptible and both sexes act as carriers.

SYMPTOMS

Most patients with sickle cell anemia are well adapted to their condition. However, questioning soon reveals that they are easily fatigued, often quite irritable and often show dyspnea on exertion. There is usually an icteric tinge to the sclera. Pallor and icterus are seen in the oral mucosa. Other oral findings will be discussed later as well as changes in the various bone structures. Leg ulcers are a common finding. The liver and spleen are usually enlarged. However, late in the disease the spleen usually becomes fibrotic and atrophied. Cardiovascular changes and pulmonary and cerebral damage are also common findings. These complications will be more fully discussed under pathology of the disease.

At unpredictable intervals, the chronic course of the disease will be interrupted by an acute exacerbation of symptoms so that the patient develops acute abdominal pains, increased jaundice, fever and prostration. These acute episodes are called "sickle cell crisis." It is at this time that the patient will seek hospitalization. The disease is not compatible with a normal life span and it is rare that the patient will live much beyond the third decade.

In the "sickle cell crisis," the acute ab-

dominal pain, high fever, and increased leukocyte count so closely mimic an acute surgical abdomen that it is not easy to make a diagnosis on clinical grounds alone. The disease has been misdiagnosed as acute appendicitis, intestinal obstruction, renal colic, acute cholecystitis, liver abscess and so on. Symptoms rarely begin before the age of six months. It is at this time that the fetal hemoglobin is replaced by sickle cell hemoglobin.

PATHOLOGY

It has been shown that the fault lies within the erythrocyte itself. In a series of experiments conducted by Singer[10] et al. it was shown that when red cells taken from a person with the sickle cell trait, are transfused into a patient with the disease, the "trait" cells survived for the normal 120 days. On the other hand, red cells taken from sickle cell patients, when transfused into "trait" carriers, survived only about 30 days. This is about the same rate at which the sickle cell patient destroys his own abnormal cells.

The nature of the abnormality within the red cells has received considerable study. It has been found that the abnormality lies within the globin portion and not the heme molecules.[15] Hb A and Hb S differ in their iso-electric points, the latter having a greater net positive charge of 2 to 4 more per molecule than normal Hb. This difference in charges may be due to a folding or coiling of the polypeptide chains which removes from action or brings into play charged groups. The net result is an indirect alteration of the electrophoretic behavior of the abnormal protein.

Although electrophoresis has become an invaluable tool in the detection of abnormal hemoglobins, other methods are now in current use as well. Some of these include differences in solubility, resistance to alkali denaturation, genetic and immunological studies, biochemical studies and so on. It has already been mentioned that Hb S has a different rate of mobility than Hb A on electrophoresis. Hence, this method is commonly used as a diagnostic test.

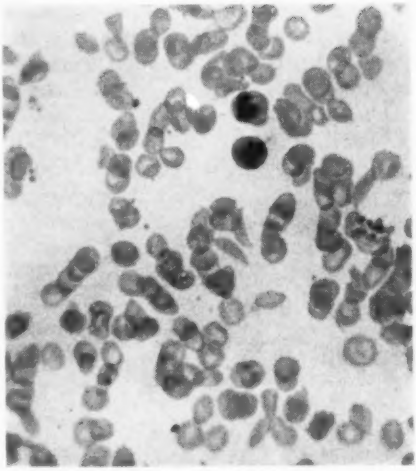

Fig. 1. (Enlarged 800 times) Wet preparation showing numerous sickle cells. These crescent shaped cells with pointed ends should be compared to normal erythrocytes in Fig. 2.

Another marked difference between Hb S and Hb A is the lack of solubility of reduced Hb S. This causes the cell to sickle and hence establishes the diagnosis as normal red cells never sickle. The test most frequently used because of its simplicity, is to place a drop of blood on a slide and exclude air from the specimen. Within 2 to 4 hours a large percentage of cells will be found to have one or more pointed ends, the classical picture being the typical crescent shape, pointed at both ends, concave on one side and convex on the other. This phenomenon occurs when the oxygen tension falls below 40 mm. of oxygen. The process can be hastened by placing a rubber band on a finger for several minutes prior to drawing the sample. An alternate method is to mix reducing agents with the sample, thus lowering the oxygen tension more rapidly.

It is known that reduced Hb S is far less soluble than reduced normal Hb A. In fact it may be only 1/100 as soluble. This causes a crystallization of the reduced Hb and the formation of long chain rod-like

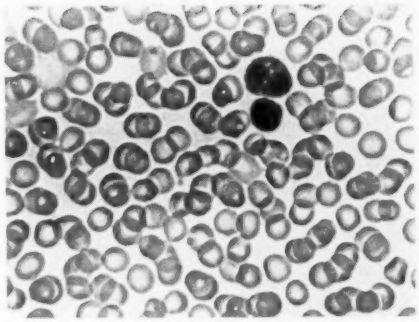

Fig. 2. Normal erythrocytes.

structures called "tactoids." It is apparently these tactoids that cause the red cell to deform. M. Price Margolies[11] who has written an admirable monograph on the subject of sickle cell anemia, has presented a series of lucid drawings of a cell undergoing the sickling process. Her monograph is quite thorough and well worth reading.

Sickling can also be produced in the trait carriers, but the oxygen tension must be lowered to 18 mm. of oxygen or less. The trait hemoglobin contains from 22 to 45% Hb S, the balance being Hb A. Apparently there is sufficient Hb A in conjunction with Hb S within the erythrocyte to prevent sickling in vivo.

It is known that the average diameter of an erythrocyte is about 7 u. In the finer capillaries, this size just about enables a normal red cell to pass through. When a cell sickles, however, it may elongate well beyond 15 u. It is obvious that a cell of such diameter cannot pass through the lumen of a capillary. As a result, the capillaries become occluded, the cells pile up, producing thrombosis, further reducing the oxygen tension, producing additional sickle cells and initiating a vicious cycle. This is aggravated by the fact that reduced Hb S is more viscous than reduced Hb A. Depending on the location of the thrombus, various organs become depleted of nutrition and suffer damage. This apparently accounts for most of the symptoms suffered by the patient.

It has also been shown that the sickle cell is mechanically fragile as compared to a normal erythrocyte. For this, and other reasons, the sickle cell undergoes hemolysis much more readily than a normal cell. Surprisingly, it is more resistant to alkalies and hypotonic solutions than a normal cell, and this fact, plus the fact that sickled cells show no rouleaux formation and do not sediment, is sometimes used to confirm the diagnosis.

It has been mentioned that many of the symptoms encountered by the patient can be explained by the marked tendency to thrombus formation. Depending on the location of the thrombus, one can readily understand the presence of leg ulcers, cardiac enlargement, brain damage, liver, spleen, lung, kidney damage and so on.

Changes in the bone patterns will be discussed in conjunction with oral findings.

LABORATORY FINDINGS

There is generally a mild to severe anemia, the red count varying from 3½ million at the upper limit, down to 1 million per cu. mm. The hemoglobin is reduced proportionately so that the color index is in the vicinity of 1. The anemia is of the normocytic, normochromic type. The marrow responds to the anemia by becoming hyperplastic and pouring into the circulation increased numbers of reticulocytes ranging from 15 to 25% of the erythrocyte count. Howell-Jolly bodies and Cabot's rings may be observed as well as nucleated red cells.[2] Some observers have reported the presence of target cells as well.

There is practically always a leukocytosis of varying degree, the count going as high as 30,000. These cells are usually mature. Eosinophilia is common, and the platelet count usually elevates. These values often reach their peak during a "crisis." Bleeding and coagulation time are usually normal.

Increased hemolysis is readily shown by the increase of fecal and urinary urobilinogen, of the serum bilirubin, largely of the

indirect fraction, jaundice, phagocytosis of the red cells by the reticulo-endothelial system, deposits of hemosiderin in the bone marrow, spleen and liver, and a regenerative blood picture.[2]

As high as 98% of the patients' hemoglobin may be of the S type, the remainder being a fetal type which is electrophoretically normal but resistant to alkalis.[12, 13]

"Because this is a hemolytic anemia, the Van den Bergh reaction shows a negative direct, and a moderately elevated indirect reaction, which usually is between 1 & 2 milligrams. During periods of crisis, when there is an increased destruction of erythrocytes, the hyperbilirubinemia increases. The icteric index is most frequently between 15 and 25 units and there is increased urobilin in the urine." (Margolies pg. 401.)

Since thrombosis is such a frequent complication of the disease the kidneys become frequently involved in this process. When this occurs, then in addition to the increase in urobilin, the specific gravity of the urine may become low and fixed, and albumin and hyaline casts may be found.

BONE CHANGES

The changes in the various bones are a result of two diametrically opposed physiological forces operating simultaneously.

On the one hand, there is an enormous stress placed on hematopoetic centers to produce more erythrocytes. The magnitude of this task we can imagine by remembering that the rate of destruction of these abnormal red cells in the patient's body permits an average life span of only 30 days. Since this is only ¼ of the normal life span of a red cell then one would imagine that at least four times as many new red cells are demanded, by the blood daily as one would find in a normal person. And even if this demand is met, the patient still shows a net deficit of between 2 to 4 million red cells per cubic millimeter. As a result of this demand, the blood producing marrow becomes hyperplastic.

On the other hand, one finds a great deal of thrombosis occurring in the capillaries of the marrow as a result of occlusion by the sickled cells. The hyperplastic marrow tends to produce osteoporosis, the thrombosis tends to produce sclerosis of the bone.

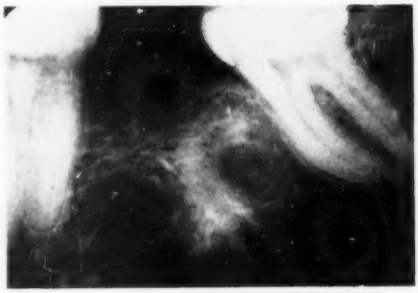

Fig. 3. Case 1 E.M. Roentgenogram showing osteoporosis and osteosclerosis occurring simultaneously.

Bearing in mind these opposing forces, one can readily anticipate the effects produced on bones.

"Congestion of the bone marrow occurs early, and areas of hemorrhage are common. As the anemia progresses, the bone marrow becomes very hyperplastic. This hyperplasia is not confined to the medullary cavity, but extends to the haversian canals as well, giving the bone a honeycombed appearance. Later, as the result of congestion and thrombosis, necrosis, hyalinization, fibrosis, abnormal calcification, and new bone formation occur."[14]

Carroll and Evans (op. cit.) have described the following roentgenologic changes that may be observed in sickle cell anemia.

A. *Long Bones*
   1. Thinning of the cortex and widening of the medullary cavity
   2. Prominent trabeculation
   3. Thickening of the cortex with narrowing of the medullary cavity
   4. Periosteal elevation
   5. Bizarre bone architecture with replacement fibrosis

B. *Skull*
   1. Osteoporosis and widening of the diploe
   2. Thickened skull, usually in localized areas
   3. Perpendicular striation

C. *Pelvis and Spine*
   1. Osteoporosis with accentuated trabeculation
   2. Biconcave vertebrae

At one time perpendicular striations of the skull, the so-called "hair-on-end" ap-

Fig. 4. Case II A.A. Roentgenogram showing osteoporosis and stepladder arrangement of trabeculae in interseptal alveolar bone. The lamina dure are very prominent.

pearance, was considered quite common in sickle cell anemia. In this condition, fine trabeculae of bone radiate from the inner table of the skull outwards. When seen on the roentgenograph, the appearance is very striking, but it is now agreed by most authorities that its appearance in sickle cell anemia is not common.

The roentgenographic changes in the jaws, especially in the series presented here, are quite striking and in accord with the findings of Sarnat and Robinson. The question arises why the changes are more apparent here than in other bones. Certainly, one cannot assume that the marrow in the mandible, for instance, plays a major role in hematopoesis and therefore responds more completely to the demand for red cells than the marrow in the long bones, for instance.

A plausible explanation is offered by Sarnat and Robinson who explain the apparent roentgenographic changes by comparing the differences in the way an intraoral film is taken, and the method used in X-raying other bones. When intraoral roentgenograms are taken, the film is placed close to the bone and relatively less soft tissue must be penetrated by the ray.

A comparison of an intraoral and extraoral film of the same region of the mouth readily shows that the intraoral film reveals much finer detail than can be achieved by the extraoral film. This situation is analagous to a comparison of an intraoral film and a film of other bones in the body.

REPORT OF A CASE

On 10/13/59 the patient E. M. was admitted to the Veterans Administration Hospital, New York, New York. This was the eleventh hospital admission of this 28 year old Negro male who enters because of severe abdominal pain. He has had a known sickle cell anemia for about seven years. Most of these admissions to the hospital are with sickle cell complaints. He states his difficulty began one hour prior to admission with sudden onset of abdominal pain radiating to the left leg anteriorly. There was no history of trauma. This was preceded by a vague feeling of malaise. For three weeks prior to admission he has had 3X nocturia and q 2 h daytime frequency. Three days prior to admission the patient noticed that the urine had become dark in color.

PHYSICAL EXAMINATION

This revealed a fairly well developed, well nourished Negro male who appeared acutely ill. Pulse 84. Blood pressure 114/62. There was scleral icterus. There were large discrete nodes bilaterally and some discete posterior cervical nodes. The rest of the physical examination was essentially normal.

LABORATORY FINDINGS

Hemoglobin 9.7 grams
Red cell count 2,760,000
Hematocrit 31%
White count 17,650
Neutrophiles 60%
Lymphocytes 30%
Eosinophiles 4%
Monocytes 6%
Reticulocytes 5% (on previous admissions this count has gone as high as 25%).
The sickle cell preparation was positive.

Fig. 5. Case III W.S. Roentgenogram showing again osteoporosis that is so intense as to give the appearance of multiple cysts.

The smear showed hypochromia, anisocytosis, toxic granulations and sickling.

Blood Urea Nitrogen 11 mgs. (normal).

Uric Acid 5.8 mg. (upper normal).

Total Bilirubin 2 mgs. with 1.2 mgs. direct (elevated).

Urine essentially negative at this time.

Electrophoresis showed over 94% Hb S.

ORAL EXAMINATION

The oral mucosae show extreme pallor and slight icterus. Melanin pigmentations, normal in the Negro race, stand out prominently. There are no periodontal pockets, the gingivae are normally stippled and the tongue presents normal papillations.

There is no lymphadenopathy and the salivary glands palpate normally. Outside of the extreme pallor, the oral mucosae and tongue are surprisingly free from any pathosis.

The teeth show no mobility. There are seven carious teeth none of which are deeply involved. Teeth numbers 23, 24 and 26 are non vital, and the dental roentgenograms show a periapical area of radiolucency around these teeth and a loss of continuity of the lamina dura in these regions.

Radiographically the maxillary osseous architecture seems to be within normal limits except between the apices of the upper left second and third molars where we see an area of radiolucency.

It is in the mandible that one sees the major portion of the abnormalities. One

Fig. 6. Case IV D.B. Roentgenogram of mandibular cuspid area showing several large osteoporotic areas.

sees large radiolucent areas, especially prominent in the regions of the premolars and molars. The marrow spaces are especially prominent and large. In contrast, the trabeculae that are still present seem quite prominent. The general pattern vaguely resembles the picture of an ameloblastoma. In the bicuspid region one can see the "step-ladder-like" arrangement of trabeculae described by Sarnat and Robinson.

Between the right first and third molars, in the edentulous space, there is a curved, very dense segment of bone probably sclerotic in nature. Just posterior to it, there is a radiolucent area, oval in outline and bounded by a circular trabeculae of bone. Even the mandibular canal begins to lose its definition at this point. However, the lamina durae do not seem to be involved in any of the osseous changes, and in fact, seem more prominent than normal, especially against the radiolucent background.

There are no evidences of infra bony pocket formation, nor any undue loss of height of the alveolar crest.

In agreement with the findings of Sarnat and Robinson when radiolucent areas are present, they involve both the alveolar bone and the mandibular bone proper.

CASE NO. 2 A.A.

In the radiographs of this case, one again sees the tremendous deviation from the normal pattern in a Negro male suffering with sickle cell anemia. The changes involve the entire mandible where the normal pattern is entirely disrupted. Radiolucent areas are also quite apparent in the upper bicuspid area. The changes here are more dramatic than in Case #1.

In Case #3, W.S., and Case #4, D.B., changes in the bony pattern of the maxilla and mandible are again very evident. The most striking radiograph is the one showing the right molar area in the mandible. Not only has the entire trabecular pattern been lost, but an examination of the inner lower border of the mandible shows a saw tooth arrangement almost as if the hyperplastic marrow had eroded the cortical plate.

SUMMARY

1. Four cases of sickle cell anemia in all of whom there were marked maxillary and/or mandibular roentgenographic changes have been studied.

2. In the study of the sickling phenomenon, new tools for the investigation of normal and abnormal hemoglobins have been developed. The hereditary nature of this, and other previously obscure hemolytic anemias has been put on a firmer basis. As a corollary, it has been found that the qualitative production of hemoglobin is under genetic control. "Today the sickling phenomenon has ceased to be the exclusive concern of the hematologist and pathologist. It has come to occupy a position at the crossroads of medicine, biochemistry, genetics and anthropology."[15]

3. From a dental standpoint, many questions still remain unanswered and deserve more intensive study. In view of the widespread thromboses found in sickle cell anemia why are so few changes found in the oral mucosa? One would expect that the end capillaries found in the gingival mucosa should logically be the seat of multiple thrombotic or infarcted areas. One might also expect widespread degenerative changes in the pulp. Since the changes mentioned above, were not a prominent finding, one is led to conclude that the oxygen tension in these tissues must have been above 40 mm. of mercury, that is, above the level at which sickling occurs. Undoubtedly, the age level of the patient is a definitely protective agent, but further study along these and other lines seems definitely indicated.

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The Periodontist and Cosmetic Dentistry

by HENRY M. SWENSON, D.D.S., AND NILES M. HANSEN, D.D.S., M.S.D.,
Indianapolis, Indiana .

COSMETIC dentistry usually is considered relegated solely to the restorative and orthodontic fields. One finds, however, that the field of periodontics also can contribute immeasurably to improving the appearance of our patients. The problems involved here may require surgical as well as prosthetic applications and are a part of the treatment which may greatly increase patient cooperation through a revived interest in dental health and appearance.

Severe gingivitis may be the cause of inflamed and at times bulbous-appearing gingivae. In such cases, thorough prophylactic treatment may achieve not only a healthy mouth but a more acceptable esthetic appearance, and a rejuvenated pride and interest on the part of the individual in his oral appearance. Dark cervical rings of calculus and stain frequently are mistaken by the patient as caries and an indication of a deteriorated dentition no longer worthy of care. The removal of these deposits from the tooth surface may be the key to a successful home-care approach.

In many cases, an improved cosmetic appearance is achieved solely by a re-contouring of tissue. Clefting of gingival tissue on the labial aspect of the mandibular incisors can be corrected by lowering the anterior frenum attachment and a localized gingivoplasty. In many such cases, food passage over this frenum causes a stretching of the gingival tissue, allowing impaction of debris around the neck of the tooth and ultimately the clefting of this area. The various forms of gingival hyperplasia are sometimes the cause of an unkept mouth as well as the effect. Frequently, a gingivoplasty will achieve a very desirable cosmetic effect and stimulate the patient to apply good mouth hygiene practices for the continued maintenance of oral health (Fig. 1).

The gingivectomy procedures commonly employed in periodontal treatment serves several purposes. By reduction of the pocket areas oral hygiene is improved, and the tooth life is prolonged. Many of these cases also achieve a renewed cosmetic harmony through the re-establishment of good, soft tissue and underlying bony contour (Fig. 2).

A recent gingivectomy patient, or the person with excessive gingival recession, may be greatly concerned by the apparent increase in the length of the clinical tooth crown. His desire to smile or laugh is repressed by the thought of his oral appearance to others. Analysis of such cases reveals that this problem is limited generally

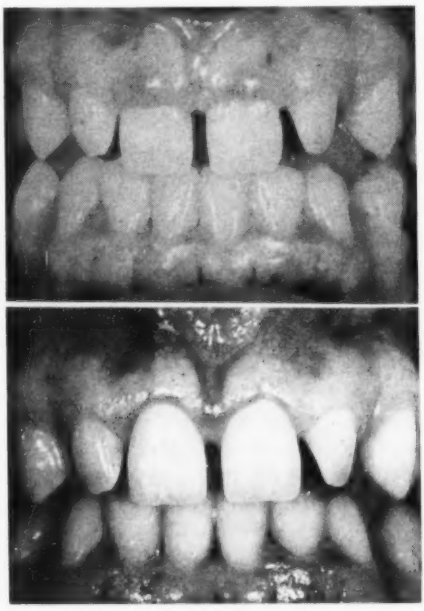


Figure 1

From the Department of Periodontology, Indiana University School of Dentistry.

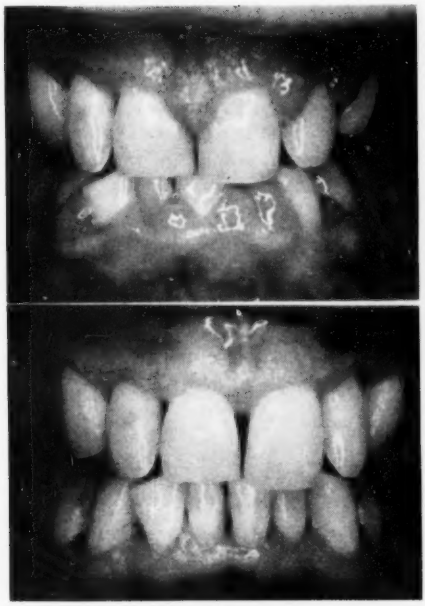


Figure 2

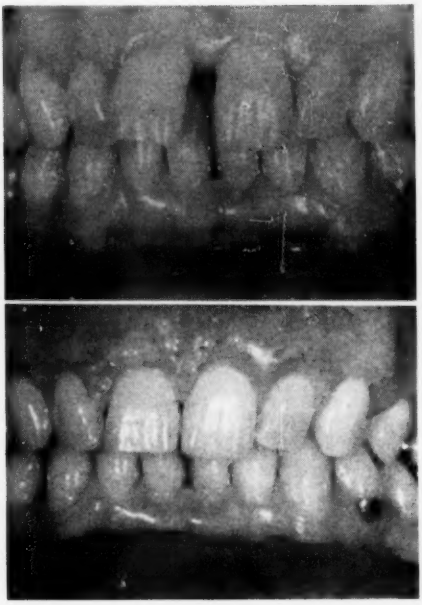


Figure 3

to the anterior portion of the maxillary arch, the cheeks and lips concealing all other areas. A simple, yet effective, correction of this problem is to be found in the cosmetic gingival prosthesis. This appliance, aside from its cosmetic value, may be useful in stabilizing mobile teeth as well as serving as a retainer. (Fig. 3) illustrates a typical case following gingivectomy, with and without such an appliance. This appliance is retained in position solely by the flexibility of acrylic and is readily removed for cleaning. When properly constructed, it has not been known to cause either discomfort or gingival irritation even after several years of use.

The construction of a labial prosthesis of this type is not difficult. Since an accurate adaptation of the acrylic to the tooth at the new gingival crest is extremely important, particular attention must be given to the interdental spaces. Open interdental spaces are noticeably large following a gingivectomy and may retain a portion of the alginate impression material after removal of the impression from the mouth. Inasmuch as one need not be concerned in this technique with an accurate impression of the lingual tooth surfaces, it has been found that placing a soft wax on the lingual of the teeth to be covered by the splint lessens the possibility of tearing the impression in the interproximal area. The wax is forced labially until an accurate impression can be taken which will provide cervical adaptation as well as sufficient retention. A stone model is poured and the case waxed up to the desired contour. The wax is stippled with a toothbrush to give the finished appliance a more natural appearing surface. It is placed then in a denture flask with the labial surface up and processed in any one of the characterized acrylics.

Occasionally, it is found that simple reduction in length of the incisal edges of the anterior teeth to make them more uniform will do much to improve esthetics. Teeth that are periodontally involved often will drift incisally, producing an unpleasing re-

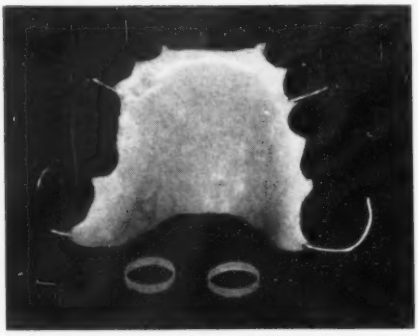


Figure 4

lationship which may be of great concern to the patient. The reduction of these teeth by careful selective grinding will not only improve the appearance of the patient but also reduce undesirable forces on the tooth.

Since drifting of anterior teeth occurs frequently in mouths with periodontal disease, many of these cases, after pocket reduction by gingival surgery, lend themselves to re-alignment by the use of some form of Hawley appliance or banding. The Hawley retainer may be the conventional labial arch wire or a combination of hooks and elastics as seen in (Fig. 4). Anterior orthodontic bands also may be used in conjunction with the elastics to provide more effective control of movement of the teeth. The bands aid in holding the elastic in the most favorable area for the desired lingual tipping type of movement.

If mesial or distal tipping is also necessary, either elastic ligature or grassline ligature may be applied in a "figure-eight" fashion across the brackets of the band. When such movement is undertaken, it is frequently desirable to position an orthodontic arch wire through the brackets to minimize the tendency of unwanted rotational movement. Changing the position of these teeth not only improves esthetics but restores normal function and makes oral hygiene easier.

Upon completion of these tooth movements, the tendency for the teeth to return to their former malalignment exists even following equilibration. Therefore, some type of fixed or removable retainer must be constructed. Pin ledge inlays, a Hawley retainer, or the cosmetic gingival prosthesis may be used effectively for the retention of these teeth. Prognosis, patient comfort, and practicability should be the guide when deciding upon a retainer. A cosmetic gingival prosthesis is used to help the retention of the teeth of the case shown in (Fig. 3).

DISCUSSION AND SUMMARY

Cosmetics in periodontal care must require serious consideration. Satisfaction in this detail may be achieved through scaling or it may necessitate surgery or prosthesis. In some instances, multiple prosthetic applications may be necessary. The prosthesis may be of either a fixed or removable nature depending on the conditions present.

Good oral hygiene can be influenced greatly by the mental attitude of the patient. The person's sense of pride in his smile is a requisite in any restorative program. The ultimate cosmetic achievement of the periodontal case, therefore, may increase the possibility of success for the satisfaction that the patient now feels makes him more receptive to a thorough home-care program. By keeping this fact foremost in mind when planning the treatment, the periodontist can do much more than to simply help preserve the supporting structures of the teeth. This phase of periodontal treatment should enhance also his colleague's work who will perform the restorative phase of the patient's care. In effect, the cosmetic considerations and their achievement in periodontal therapy may be the deciding factor for successful treatment.

Roy O. Elam, Sr., D.D.S.

November 30, 1960

DR. ROY OSCAR ELAM, SR.

Dr. Roy Oscar Elam, Sr., past president of the Academy of Periodontology and the Tennessee State Dental Association, died November 30 in a Nashville hospital of a stroke. He was born in Greenfield, Tennessee, Weakley County, and was graduated in 1919 from the Vanderbilt University School of Dentistry. He was a member of Omicron Kappa Upsilon honorary fraternity, Psi Omega and Phi Kappa Sigma fraternities. He was married to the former Elizabeth Southgate of Nashville.

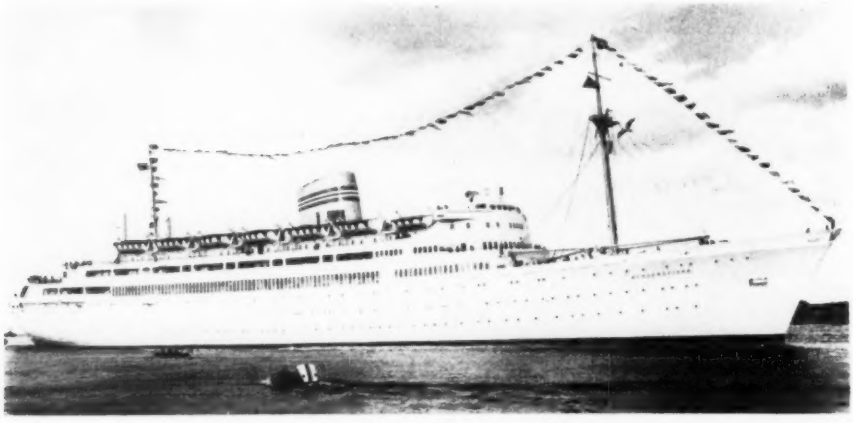
Dr. Elam began his dental practice in Columbia after graduating, and moved to Nashville in 1922, where he maintained his practice until his retirement in 1957. He had from time to time held every office in the Nashville Dental Society, and also served for three years on the Legislative Committee, and three years on the Judicial Committee of the American Dental Association. For nine years, he served on the Council on Dental Education of the A.D.A.

The Annual Meeting of the Tennessee State Dental Association in 1959 was dedicated to him. The convention tribute praised Dr. Elam for "his efforts toward making dentistry a better and more highly respected profession, his service to dental organizations, his skill, his fellowship and his wise counsel."

Dr. Elam was a member of St. George's Episcopal Church, Nashville. He was a Fellow of the American College of Dentists and the International College of Dentists. Surviving, besides Mrs. Elam are two sons and one daughter, Dr. Roy O. Elam, Jr., Bernard Elam and Mrs. Bernard Evers, Jr., all of Nashville and ten grandchildren.

Announcements . . . .

NEXT ANNUAL MEETING OF THE AMERICAN ACADEMY OF PERIODONTOLOGY TO BE A CRUISE



The 47th annual meeting of the American Academy of Periodontology will be held October 20-25, 1961, aboard the M.S. Bergensfjord. Various A.A.P. committees have planned five days of a combination of business and pleasure beginning at the Philadelphia docks any time between 8 a.m. and 11 a.m. on Friday, October 20. The 18,750 ton M.S. Bergensfjord is a new pleasure boat which is fully air-conditioned, equipped with the latest stabilizers and with ample facilities for all types of sports, sun bathing and loafing.

State rooms are furnished in modern Scandinavian style and include complete facilities. The cuisine, although eminently international, has the added zest of world-renowned buffet specialties which have made Norway the gourmet's delight, and six meals are served each day.

Details of the scientific program will be made available later, but since space on the Bergensfjord is limited, reservations should be requested at once. The Caribbean Cruise Lines manager is Mr. E. M. Baskette, Suite 301 Roper Building, Miami 32, Florida. Additional details may also be obtained by writing the Secretary of the American Academy of Periodontology, Dr. Clarke Chamberlain, 1101 North Street, Peoria, Illinois.

PROGRAM FOR THE SPRING SEMINAR OF THE AMERICAN ACADEMY OF PERIODONTOLOGY

April 24-26, 1961

The annual Spring Seminar of the American Academy of Periodontology will be held this year in Ann Arbor, Michigan, Monday, April 24 through Wednesday, April 26. Anyone interested may get details by writing Dr. Donald M. Kerr, University of Michigan School of Dentistry, Ann Arbor, Michigan, or Dr. Clarke Chamberlain, Secretary of the Academy, 1101 North North Street, Peoria, Illinois.

Monday, April 24

A.M.

8:30 - 9:30 Registration

9:30 - 12:00 Wound and Bone Healing
DR. WILLIAM G. SHAFER
Professor and Chairman of the Department of Oral Pathology, Indiana University, School of Dentistry

P.M.

1:30 - 4:30 Diagnosis and Treatment of Pain in the Head and Neck Regions
DR. JANETT TRAVELL
Associate Professor of Pharmacology, Cornell University Medical College

Tuesday, April 25

A.M.

9:00 - 12:00 Stomatitis
DR. DONALD A. KERR
Professor and Chairman of the Department of Oral Pathology and Periodontics, The University of Michigan, School of Dentistry

P.M.

1:30 - 4:00 Applications of Psychiatry to Dental Practice
DR. LEONARD E. HIMLER
Associate Professor of Mental Health, The University of Michigan

Wednesday, April 26

A.M.

9:00 - 12:00 The Present Status of Conservative Periodontal Therapy and Reattachment
DR. ERWIN M. SCHAFFER
Professor and Chairman of the Department of Periodontics, University of Minnesota, School of Dentistry

P.M.

1:30 - 3:30 The Present Status of Bone Surgery in Periodontal Therapy
DR. FRANK M. WENTZ
Professor and Chairman of the Department of Periodontics, Loyola University, School of Dentistry, Chicago

COLLEGE OF MEDICAL EVANGELISTS

The School of Dentistry of the College of Medical Evangelists, Loma Linda, California, announces a postgraduate course, "Periodontics for the General Practitioner" to be presented March 5 to 7, 1961.

This three-day course will consist of two days of lectures and discussion and one day of clinical demonstrations. The presentation is directed toward the inclusion of modern periodontic concepts and techniques in the general practice of dentistry. The course content will include histology of the periodontium; classification and diagnosis of periodontal diseases; examination, charting, treatment planning; factors in the prognosis; case presentation; periodontal therapy; occlusal adjustment by selective grinding; stabilization of loose teeth; periodontal surgery; maintenance phase of treatment; sharpening of instruments. Techniques to be demonstrated on patients are as varied as time and choice of patients allow.

The guest lecturer will be Dr. B. O. A. Thomas, Clinical Professor of Periodontics at the College of Physicians and Surgeons in San Francisco, lecturer in anatomy at Stanford University, and private practitioner in Palo Alto, California.

The fee for this course will be $65 and enrollment will be limited.

For further information regarding this course write to Chairman, Graduate and Postgraduate Dentistry Committee, CME School of Dentistry, Loma Linda, California.

TUFTS UNIVERSITY

Tufts University School of Dental Medicine announces the following refresher courses:

February 8 to April 5, 1961. Orthodontic Principles of Interest to the General Practitioner. Each Wednesday for eight weeks. Tuition $200.00.

April 24 to April 28, 1961. Participation Course in Periodontology. Tuition $175.00.

May 3 to May 5, 1961. Clinical Adjustment of the Occlusion. Tuition $125.00.

May 23 and 24, 1961. Diagnosis and Treatment of Pain and Other Symptoms Arising from Temporomandibular Joint Disturbances. Tuition $75.00.

For further information write Director, Graduate and Postgraduate Division, School of Dental Medicine, Tufts University, 136 Harrison Avenue, Boston 11, Massachusetts.

BALINT ORBAN MEMORIAL SEMINAR

The Rocky Mountain Dental Seminar will hold its second session, in memory of its founder, Dr. Orban, in Boulder, Colorado, June 25th to 28th, 1961. Theme for the Seminar is "Clinical and Microscopic Pathology of the Periodontium and Other Oral Structures." The outstanding group of essayists includes: Dr. S. N. Bhaskar, Dr. Henry Goldman, Dr. Maynard K. Hine, Dr. Harry Sicher.

Further details and application form may be obtained by writing to Virginia B. Manella, Secretary, 1700 Mesa Rd., Colorado Springs, Colorado.